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A.M.A. ARCHIVES OF NEUROLOGY & PSYCHIATRY

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Paul D. MacLean

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II. Behavioral Findings

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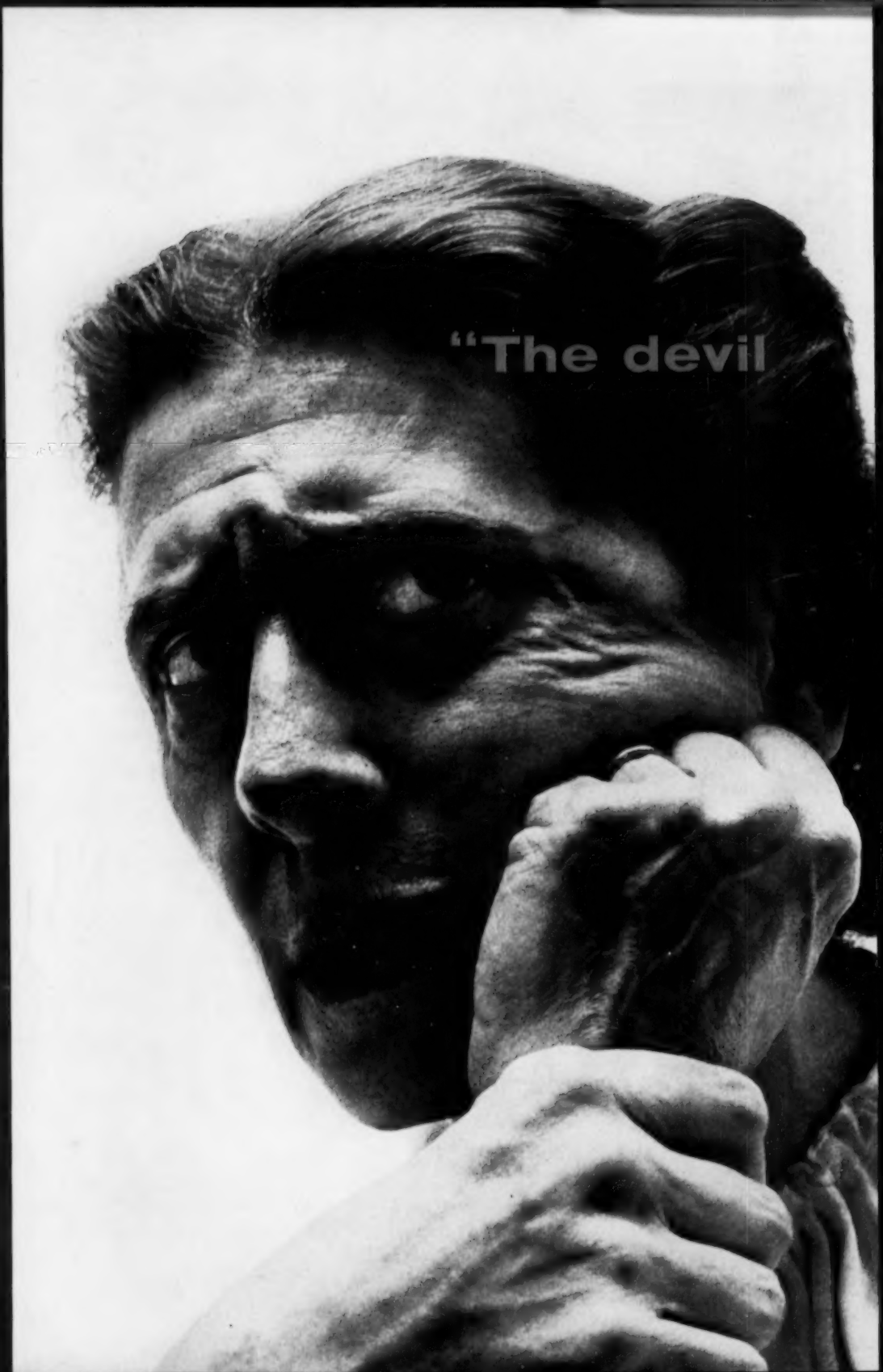
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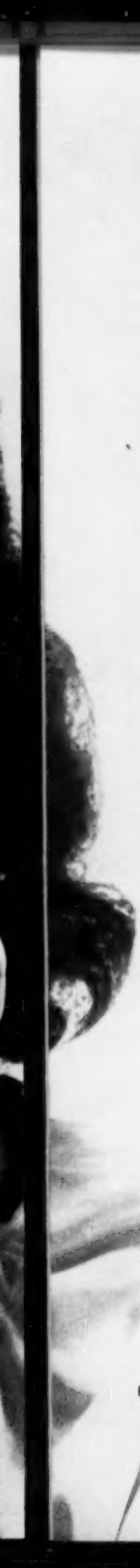

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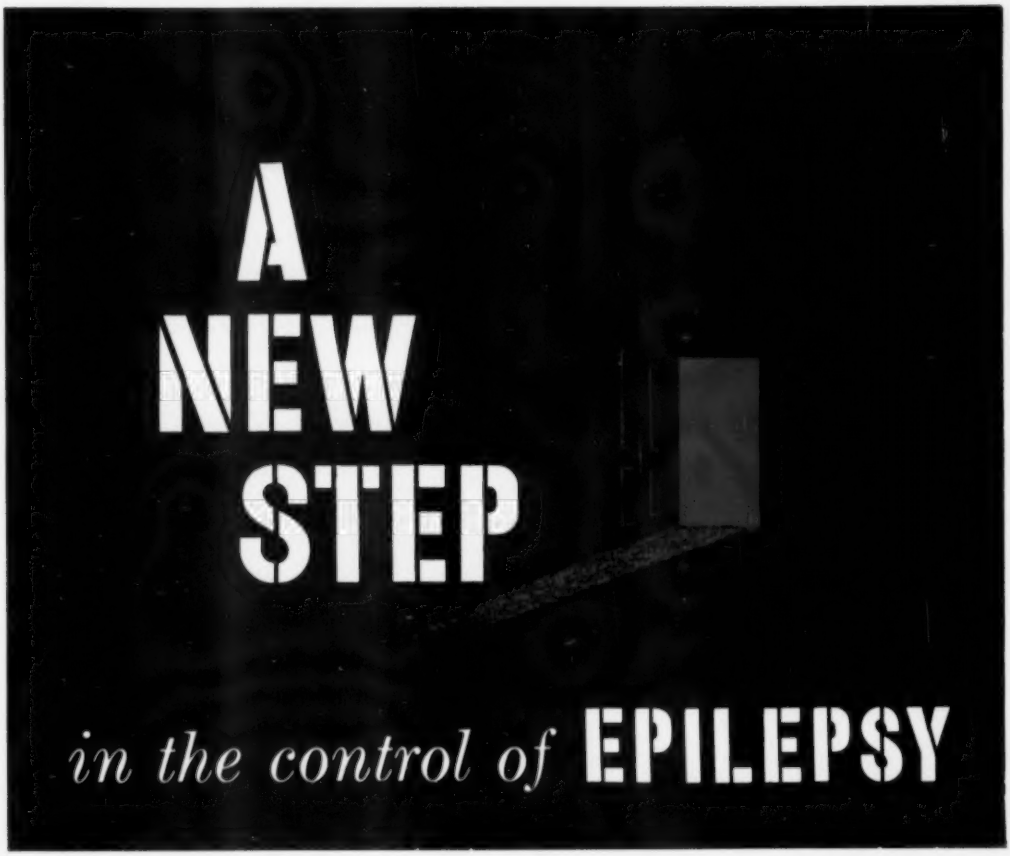

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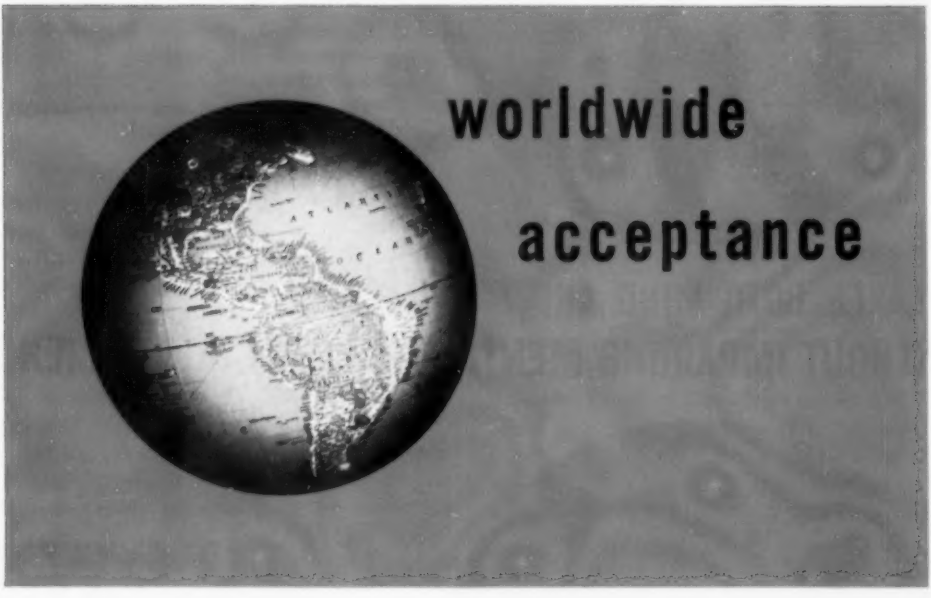

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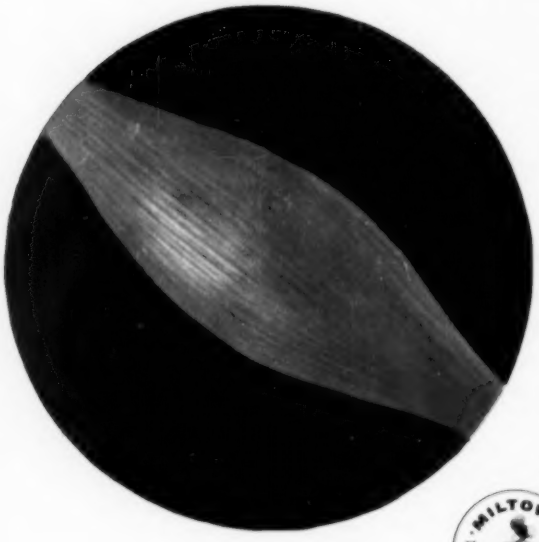

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SECTION ON
NEUROLOGY

Chemical and Electrical Stimulation of Hippocampus in Unrestrained Animals

I. Methods and Electroencephalographic Findings

PAUL D. MacLEAN, M.D., New Haven, Conn.

In recent years there has been increasing interest in the role of the phylogenetically old cortex in viscerosomatic and emotional functions and in psychomotor epilepsy. The phylogenetically old cortex comprises the so-called archicortex and mesocortex. The archicortex and the greater part of the mesocortex are contained in the limbic lobe, which is found as a common denominator in the brains of all mammals. The "old" cortex and its associated nuclei constitute a functionally integrated system, which may be appropriately referred to as the limbic system.[36]

Most of the archicortex is folded into the large cerebral convolution known as the hippocampus, or cornu ammonis. In addition to its cytoarchitecture, the hippocampus is distinguished from the rest of the brain by its peculiar, primitive end-arterial type of blood supply. It also possesses quite distinctive bioelectrical and biochemical properties (see MacLean[38,39] for review and references). Clinical, anatomical, and physiological observations have suggested hypotheses as to the role of the hippocampus in memory, learning, and affective behavior,[21,35,45] but definite knowledge of its functions is lacking.

In the course of studying the function of respective parts of the hippocampus and of related structures, my colleagues and I have employed a method that allows one to stimulate electrically or chemically * the same point in the brain and at the same time to observe the electroencephalographic and behavioral changes in the unrestrained and waking animal. Several hundred observations have been made in a series of studies that have thus far focused attention on the hippocampus, the cingulate cortex,[26,31] the hypothalamus,[14,58] the septal region,[58] and the caudate nucleus.[57] This and the following communication (Part II) will deal with the results of a study on the hippocampus

Received for publication Aug. 10, 1956.

Associate Professor of Physiology.

Department of Physiology, Yale University School of Medicine.

Aided by research grants from the Foundations' Fund for Research in Psychiatry; the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, U. S. Public Health Service, and the National Science Foundation.

* The use of local chemical stimulation of the brain to induce behavioral changes has an extensive history. As long ago as 1887, Landois demonstrated that the application of creatine and other substances to the frontal cortex of one side evoked convulsive movements of the opposite side of the body.[29] Since then, a wide variety of chemicals, including calcium-precipitating salts, convulsants, and choline derivatives, have been used for the purpose of stimulation. Masserman employed a method that allowed the comparison of the effects of electrical and chemical stimulation of the same locus in the brain.[48]

in which the foregoing method was devised and put to test. Some of the findings have been reported elsewhere.[38-40] The experiments were performed in cats and involved an intermediate segment of the hippocampus lying in the groove between the medial and lateral geniculate bodies and located approximately between frontal planes A1.5 and A4.5 of Horsley-Clarke coordinates. Because of the nearly vertical course of the hippocampus at these levels, a larger portion of this structure was explored than the foregoing coordinates would indicate.

In a previous investigation on the frontotemporal portion of the limbic system,[37] local chemical stimulation with acetylcholine was used in one group of animals in an attempt to control a number of affective responses elicited in another group by electrical stimulation. When such responses were obtained by the latter method, there was the possibility in some instances that they were the result of stimulating pain fibers of the dura, blood vessels, or Gasserian ganglion in the neighborhood of the electrodes. Acetylcholine was chosen as the chemical agent because, in addition to its being a naturally occurring substance in the brain, there was previous experimental evidence that upon topical application it was an effective stimulant [17] and that it activated directly the bodies of nerve cells but not their axons.[33]

In the present study, there was another reason for employing acetylcholine and a number of related compounds. The high choline acetylase activity in the hippocampus that was reported by Feldberg and Vogt [16] suggested that acetylcholine might play a particularly significant role in neural transmission in this structure. There was the possibility, therefore, that prolonged cholinergic † stimulation of the hippocampus might bring about behavioral changes over and above the meager responses that were initially seen when using electrical stimulation.

In addition to those already mentioned, there are three other considerations that make the foregoing form of chemical stimulation a desirable adjunct to electrical stimulation in the study of functional localization: 1. It circumvents the stimulation of fibers of passage. 2. It precludes antidromic stimulation, an eventuality that could conceivably lead to the suppression of function in structures that might otherwise be active participants in a response. 3. It allows one to observe for a prolonged period of time the induced electroencephalographic and behavioral changes.

Attention was focused particularly upon the effects of acetylcholine (in conjunction with physostigmine), methacholine (Mecholyl), and carbachol (Doryl). It will be emphasized that the method of applying these agents avoids some of the disadvantages of injecting drugs in solution.

Materials and Methods

Behavioral observations were made on 28 cats. Simultaneous electroencephalographic recordings were obtained in 18. Supplementary electroencephalographic data were obtained from acute experiments on 14 cats. The present investigation, which was begun in February, 1952, has provided background for a variety of collaborative studies on the effects of hippocampal stimulation that have involved over 40 cats, as well as a number of rats, rabbits, and monkeys. Occasional reference will be made to this material.

Methodological Considerations.—In behavioral studies employing chemical stimulation, the exciting agents have commonly been injected into the brain in solution in amounts as great as or greater than 0.1 cc. Realizing that the nonyielding character of brain tissue precludes the localized deposit of such large amounts of fluid, we limited the quantities of acetylcholine solutions injected in a previous study to 0.01-0.02 cc.[37] In the present investigation, it was found that even these small quantities will not remain localized, but tend to follow the path of least resistance along the shank of the needle. Where the needle makes a shallow penetration of structures lining the ventricular system, part of the injected material will therefore escape into the cerebrospinal fluid. In preliminary experiments, when this complication occurred upon injecting the hippocampus with cholinergic drugs,

† In the strict sense, the terms cholinergic and adrenergic apply only to classes of nerves. As Goodman and Gilman point out, however, it has become common practice to use them for other adjectival purposes.[18]

there resulted a characteristic syndrome in which the animal circled to the opposite side and manifested angry behavior and other symptoms that will subsequently be described in Part II. In acute experiments in which the hippocampus was exposed and injected under direct observation, it was demonstrated that the use of a viscid substance as a vehicle did not prevent the reflux of the injected material into the ventricle. This complication could be circumvented, however, if the chemical agents were deposited in solid form. It was also found that this provided a more effective means of inducing neural excitation in the hippocampus.

Method of Electrical and Chemical Stimulation. This method allows the principle of stereotaxis to be applied in unrestrained and waking animals. It involves the implantation of needle guides in the skull of the animal through which insulated needles with lead-off wires can be subsequently introduced to desired points in the brain without the use of anesthesia. One calculates the length of the needle to be used on the basis of Horsley-Clarke coordinates. The substances to be deposited in the brain are tamped into the tip of the injecting needle. The quantity can be approximately estimated by noting the distance through which the stylet in the needle is displaced and then making calculations on the basis of the known diameter of the needle. In order that the exciting agent will not come in contact with fluid and tissue in the pathway of the needle, the tip of the needle is sealed with some relatively inactive substance. After the needle is introduced and fixed to the guide, the substances may be allowed to dissolve and diffuse out in situ, or they may be ejected by the stylet.

The needle guides, which just penetrate the thickness of the skull, are implanted by means of a Horsley-Clarke instrument. They are fixed in place by a plastic dental cement. Upon closure of the skin incisions, they protrude several millimeters above the scalp. In the present experiments, they were constructed of No. 18-gauge stainless steel tubing, which just allows the passage of an insulated No. 22 needle.

The specially constructed injecting needles are insulated with three coats of a special abrasion-resistant paint.‡ A short length of India rubber tubing is fitted over the light and slender hub of the needle so that it extends down the shaft of the needle a distance of 2 or 3 mm. Upon injection, this rubber embraces the needle guide and thereby secures the needle so that the animal cannot shake it out.

‡E. I. du Pont deNemours & Co., Inc., supplied this paint, which has the code number 828-014.

If desired, straight, tapered, stainless steel needle electrodes may be permanently implanted 2 mm. apart in various parts of the brain for purposes of bipolar recording and stimulation. They protrude above the scalp in the same manner as the needle guides and may be connected to lead wires by miniature connectors. The needle guides and implanted needle electrodes are reinforced above the scalp by being made an integral part of a platform of plastic dental cement, reinforced in turn by embedded metal screening.

The light, flexible leads from the intracerebral electrodes, as well as those used for recording the EKG, are connected at the time of an experiment to a small connector assembly fixed to the back of the animal by means of a harness. A multilead cable passes from the connector assembly to the recording and stimulating apparatus.

Recording and Stimulating Apparatus.—Brain potentials were recorded by a Grass ink-writing electroencephalograph and an electronically switched double-beam cathode-ray oscillograph. Electrical stimulation was performed with a Grass stimulator in conjunction with an R. F. isolation unit.

Precautionary Measures.—After the guides were implanted, at least two days were allowed for the animal's recovery before undertaking experimentation. Prior to introducing an injecting needle, the dura was punctured by a sharp needle passed through the needle guide. After testing the animal's behavior following this procedure, the injecting needle was introduced and fixed in place. (With gentle handling, the animal submits quietly to these manipulations.) The present experiments were semiacute in nature, and to avoid deterioration in the state of the animal, it was found advisable to attempt no more than four chemical injections in one preparation. These were usually done in the morning and afternoon, respectively, of the third and fourth postoperative days. (If chronic experimentation is contemplated, the animal should be treated with antibiotics, e. g., chlortetracycline, or (Aureomycin.) It was the practice to make no more than one injection through the same needle guide. The reasons for this were threefold: It facilitated the microscopic identification of the exact locus of injection; it lessened the danger of causing bleeding and excessive tissue damage; it assured that the tip of the needle would be snugly surrounded by tissue, a situation that militates against the spread of the chemical along the needle tract.

Spread of Chemicals in Brain.—In employing electrical stimulation, one is concerned with the extent of spread of the current. With chemical stimulation, a corresponding problem is to estimate the extent of spread of the injected substance. In order to get a first approximation of such a

spread, observations were made on the spread of dyes in brains of living preparations. When powdered Nile blue was deposited in cortex in a quantity comparable to the amounts of cholinergic drugs employed in the present studies, it spread little more than a radius of 1 mm. in 40 minutes. Spreading factor (hyaluronidase) failed to enhance appreciably the spread of dyes. This observation was in agreement with the unpublished findings of Duran-Reynals.[10] To get a further approximation of the spread of chemicals, Lockhart, in a study to be reported elsewhere, deposited a mixture of equal quantities of Nile blue and radiophosphorus in cortex.[81] It was shown by radioautographic and by counting techniques that, although its pattern of spread was different, radiophosphorus diffused but little farther than the dye.

Verification of Site of Stimulation and Pathological Study.—In order to obtain both the gross and the microscopic picture of the pathological changes, as well as to identify the sites of the electrodes, the experimenter cut his own serial sections. Except in one case in which there was an extensive suppurative meningitis, infection was not a significant complication in these semiacute experiments. In some instances small hemorrhages were seen extending into the white matter at some points along the course of the needle tract. Usually, however, the needle made a relatively clean course through the brain tissue and left a small track (Fig. 1). Microscopic examination showed red blood cells filling the track and a moderate number of polymorphonuclear leukocytes and Hortega cells infiltrating both the site of the track and the surrounding tissue. In most instances the area at the tip of the needle showed but relatively few polymorphonuclear leukocytes and Hortega cells. As illustrated in Figure 1, some loss and paling of nerve cells were noted in the region of the tip of the electrode. Such changes were more clearly discernible in experiments employing carbachol than in those in which acetylcholine was used, a finding that is possibly to be correlated with the greater intensity and duration of the carbachol-induced seizure (see below). As is also illustrated, there was loss of nerve cells up to 0.5 mm. away from the track at the point where the needle entered, and presumably dimpled, the hippocampus.

Fig. 1.—Microscopic section showing extent of needle track in hippocampus in a typical experiment. Note loss of cells at point where needle entered, and presumably dimpled, the hippocampus. In this particular experiment crystalline carbachol was deposited by the needle. Note paling of the cells below lower end of track.

Results

I. EEG Findings in Anesthetized Animals

1. *Acetylcholine and Methacholine.*—These observations were made with direct exposure of the hippocampus in the course of resolving technical problems already referred to in the section on "Methods." In the animal under pentobarbital (Nembutal) anesthesia, persisting EEG changes were not regularly obtained with acetylcholine and methacholine unless these drugs were deposited in the hippocampus in concentrated form and unless physostigmine was applied in conjunction with the former. The changes appeared after a minute or more and were first manifest by low-voltage ripple-like activity at a frequency ranging from 20 to 30 per second. During the next few minutes, there was a slowing of this oscillatory activity to a frequency of 14 to 16 per second and an increase in its amplitude to 50μv to 100μv. The electroencephalogram had the appearance of u's or n's written in continuation. With acetylcholine, this activity, sometimes interspersed with spike-like potentials up to 300μv, gradually subsided during the course of 20 minutes. With methacholine, the changes might persist for more than double that time.

2. *Carbachol.*—Figure 10 illustrates the nature of seizure activity induced by carba-

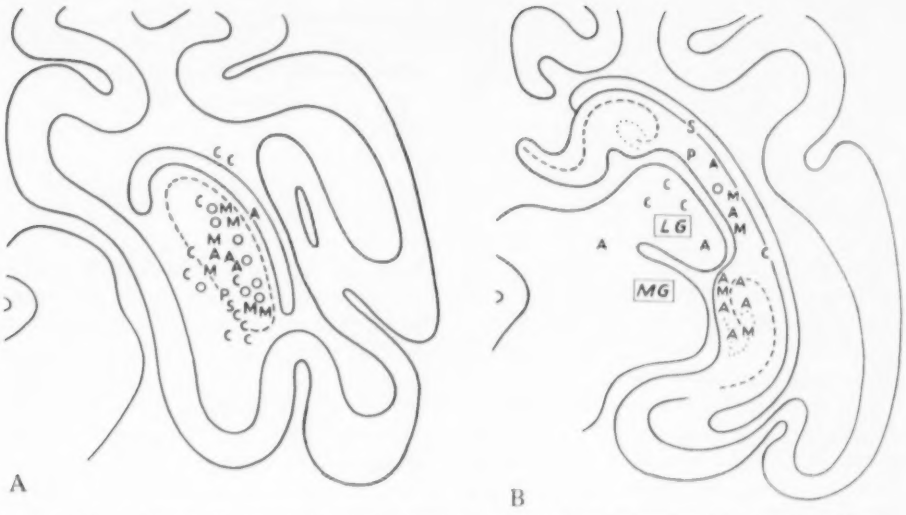


Fig. 2.—Sites of stimulation and recording projected on representative cross sections through part of hippocampus under study. *A* and *B*, respectively, correspond approximately to frontal planes A2 and A4 of Horsley-Clarke coordinates. Letters refer to crystalline agents applied in injecting needles. *A*, acetylcholine; *M*, methacholine; *C*, carbachol; *P*, penicillin; *S*, sucrose; *O*, empty needle. *LG*, lateral geniculate body; *MG*, medial geniculate body. Broken and dotted lines correspond, respectively, to cellular layers of hippocampus and dentate gyrus.

chol in an animal anesthetized with chloralose and urethan. It was characterized by oscillatory potentials at a frequency around 20 per second, which subsequently became interspersed with spike potentials. These changes lasted several hours. The amplitude of the seizure activity (around 400μv) did not begin to approach that seen in the unanesthetized animal (see below).

II. EEG Findings in Unrestrained and Waking Animals

Electroencephalographic observations were made on 18 cats. In Figure 2 the sites of stimulation and recording are projected on two representative cross sections through the region under study. Rostral and caudal to these levels there were an additional 12 sites at which recordings and stimulations were made in various subcortical structures.

With the relatively large electrodes used in these experiments, the electroencephalographic picture seen in the cathode-ray oscilloscope was essentially similar to that recorded by the ink writer. Illustrations will be taken from records obtained with the ink writer.

1. *Hippocampal Injury Discharges.*—In keeping with the findings of Renshaw et al.[69] and others,[2,30] injury discharges, similar to the one illustrated in Figure 4, were typically seen when the needle electrodes entered or impinged upon the hippocampus. In the majority of instances these discharges lasted from 20 to 34 seconds (mode, 24 seconds), with voltages ranging from 500μv to 1000μv. Following the injury discharge, the tracing became practically flat and then gradually recovered the appearance ordinarily seen during resting activity.

2. *Resting Activity of Hippocampus.*—A sample of the activity of the hippocampus recorded with an empty injecting needle is shown in Figure 3. The activity usually shows random fast potentials of low to moderate voltage, with some regular and irregular activity at a frequency of 3 to 5 per second and amplitudes up to 200μv interspersed. Bursts of quite regular activity with a frequency of close to 4 per second are commonly seen when the animal shifts

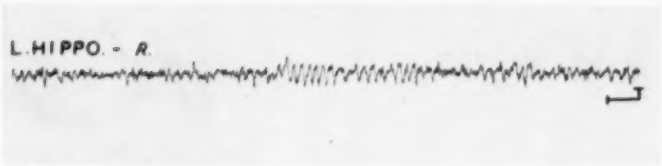
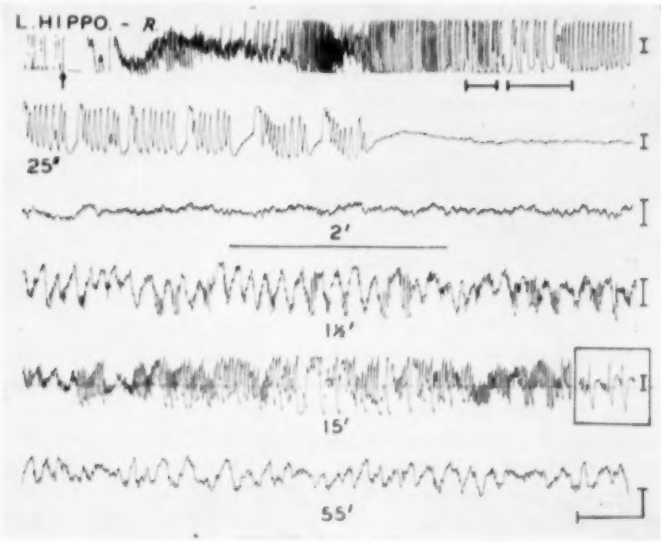


Fig. 3.—Sample of resting activity of hippocampus recorded with an empty injecting needle. See text for description. Calibrations, one second and 100μv. *R*, in this and in subsequent figures, denotes reference lead.

or focuses its attention or is aroused by an external stimulus.[19,30] Auditory stimuli may evoke spike potentials of 70μv-150μv. As reported by others, there is a rapid adaptation to a series of such stimuli.

3. Acetylcholine.—Acetylcholine chloride, in amounts of 0.03-0.06 cu. mm., was deposited in the hippocampus on nine occasions (Fig. 2). A dose of 0.06 cu. mm. weighs approximately 50γ. The tip of the injecting needle was usually sealed with physostigmine, which was allowed to dissolve and diffuse out at the site of injection for several minutes. If this was not done, acetylcholine failed to elicit the sustained and well-developed electroencephalographic changes illustrated in Figure 4. The application of physostigmine by itself results in no distinctive alteration of the EEG; but when it is followed by acetylcholine, changes may be evident within 30 seconds. They are manifest as fast potentials of low voltage that appear like ripples on the record. Within another minute (Fig. 4) the changes are clearly discernible and are characterized by bursts of regular activity with frequencies around 30 per second and with voltages gradually increasing in amplitude up to 100μv to 200μv. At the same time, there may be an increase in background rhythmic activity at a frequency of about 4 per second. As the fast oscillatory activity becomes more

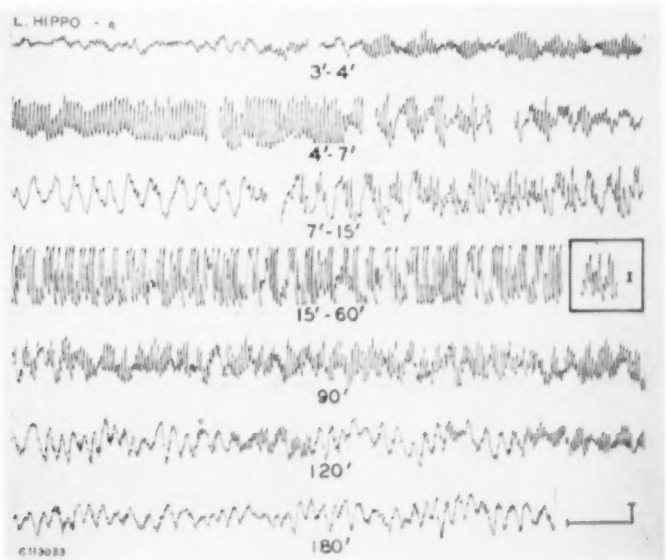
Fig. 4.—Electroencephalographic excerpts from an experiment in which crystalline acetylcholine and physostigmine were deposited in hippocampus. Top three tracings illustrate injury discharge and subsequent flattening of the record that are typically seen when needles enter or impinge upon hippocampus. Acetylcholine was ejected from the needle several minutes after physostigmine, sealing tip, was allowed to dissolve in situ. Tracings below solid line illustrate the changes that followed. Calibrations, one second and 200μv; negativity upward.



conspicuous, it begins to be interspersed with high-voltage spikes. In some experiments the first major deflection of these spikes was positive; in others, negative. In about 15 minutes this spiking activity becomes a striking feature of the record (Line 5). The spikes usually did not exceed 700μv, but in one experiment they reached 1200μv and occurred fairly regularly at 8 per second for a period of several minutes. As the spiking activity begins to abate, rhythmic activity around 3 to 4 per second, with superimposed fast potentials of low voltage, again becomes conspicuous. Usually by the end of an hour the drug-induced changes are little, if at all, in evidence. No EEG changes were observed when acetylcholine was deposited in the fimbria.

4. *Carbachol.*—Carbachol was deposited in amounts of 0.03 or 0.06 cu. mm. The tip of the injecting needle was usually sealed with glucose or sucrose, and occasionally with physostigmine. In the amounts used, these sealing substances produce by themselves no discernible alteration of the EEG. In many respects, the nature and sequence of the EEG changes following carbachol are comparable to those that have been described for acetylcholine. Two to four minutes after the drug is ejected by the stylet, rhythmically recurring potentials at about 20 per second begin to appear in the EEG, and, as illustrated in the top line of Figure 5, are frequently grouped in the form of spindles. Subsequently they increase in amplitude up to 600μv and may occur in long trains. Intermittently thereafter, this fast oscillatory activity may be largely replaced by rhythmically recurring slow potentials, at around 3 per second. At such times (Line 2) the fast potentials tend to group themselves on the falling phase of these slow waves. Seven to fifteen minutes after the drug is deposited, high-voltage spikes begin to appear interspersed among the fast oscillatory activity. For the next 45 to 60 minutes these spiking potentials (Line 4), reaching 1400μv to 1600μv, become the dominant feature of the record. They may occur continuously, with varying frequencies of 7 to 10 per second, throughout this period. After this prolonged and intense

Fig. 5.—Excerpts showing development, culmination, and subsidence of seizure activity induced by deposit of crystalline carbachol in hippocampus. Excerpt in box shows activity in Line 4 as it appears with reduced gain of amplifier. Calibrations, one second and 200μv.



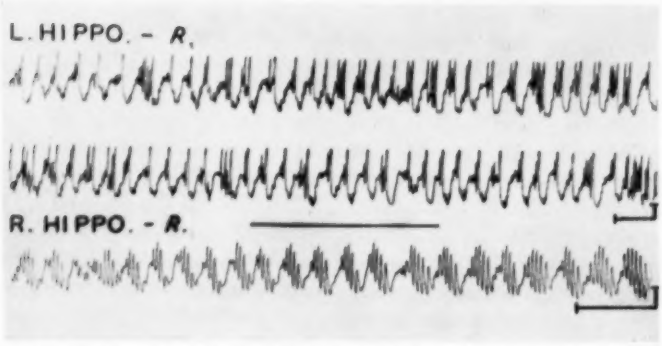


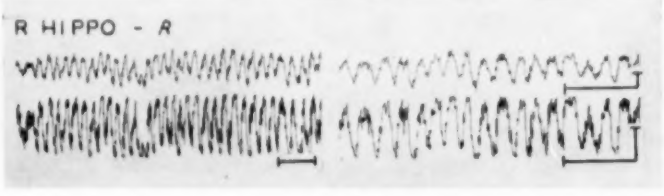
Fig. 6.—Records from two other experiments employing carbachol, illustrating slow rhythmic activity with superimposed fast potentials that occur for long periods during subsiding phase of carbachol seizures. Note how the spike and fast oscillatory potentials tend to group themselves near the peak and on the falling phase of the slow waves. Compare with incipient stage of carbachol seizure shown in top tracings of preceding figure. Calibrations, one second and 200μv.

discharge, the "seizure" gradually subsides during the next hour or two, dissipating in the same patterns of activity that characterized its development. As illustrated in Figure 6, taken from experiments on two other cats, background rhythmic activity at 2 to 2.5 per second may be conspicuous during the period of the abating seizure. These records also illustrate how the spike and oscillatory potentials tend to group themselves near the peak and on the falling phase of the rhythmic slow waves. As illustrated in the last line of Figure 5, as the spiking and fast rhythmic potentials disappear, rhythmic activity around 3.5 to 4.5 per second becomes the dominant feature of the record.

5. *Methacholine.*—Methacholine chloride or methacholine bromide was deposited into the hippocampus on eight occasions, usually in the amount of 0.03 cu. mm. The tip of the needle was sealed with physostigmine or sucrose. It is to be emphasized that the spiking activity associated with acetylcholine and carbachol never developed in these experiments. Rather, the only notable change was a marked increase in the background rhythmic activity at about 4 per second, with superimposed oscillatory activity at about 35 per second. Figure 7 illustrates the nature of these changes. They appeared and disappeared so gradually that it was difficult to estimate their time of onset and duration. They were clearly discernible only during the first hour following the application of the drug.

6. *Other Drugs.*—The deposit of crystalline penicillin G (potassium salt) in the hippocampus resulted in the appearance of randomly occurring spikes with voltages up to 700μv (Fig. 8). These spikes seldom occurred more frequently than once per sec-

Fig. 7.—Experiments employing crystalline methacholine were characterized by the appearance of persisting rhythmic activity of the type shown above. With increased gain of amplifier (bottom tracing) one could clearly detect the presence of superimposed fast activity at a frequency of about 35 per second. Calibrations, one second and 200μv.



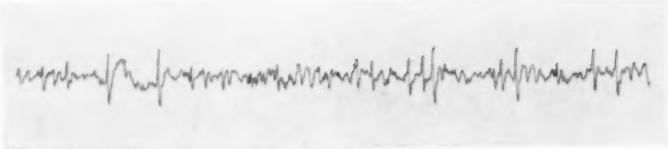


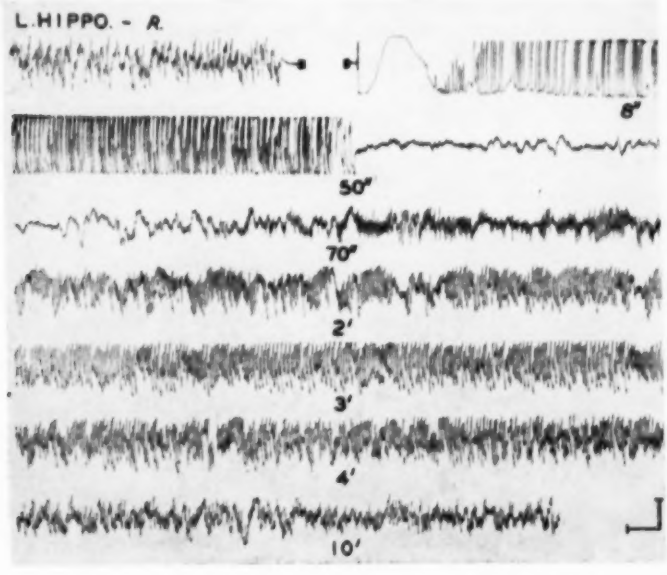
Fig. 8.—Tracing showing randomly occurring spikes in hippocampus following application of crystalline penicillin. These potentials were present for two hours and reached an amplitude of 700μv.

ond and gradually disappeared from the record during the course of two hours. Crystalline arterenol elicited no significant electroencephalographic changes in the hippocampus or in other cerebral structures.

7. *Post-Tetanic Reactivation of Chemically Induced Activity.*—On several occasions, when acetylcholine-induced changes were beginning to subside, it was observed that electrical stimulation through the injecting needle brought about a prolonged resurgence. Electrical stimulation was usually applied for 10 seconds with the stimulator set to deliver 1 msec. pulses at a rate of 60 per second. When the voltage was below that required for inducing an after-discharge, an increase in the drug-induced activity was barely detectable. But, as illustrated in Figure 9, following an after-discharge there was a marked recrudescence, which would last as long as 9 or 10 minutes. In this particular experiment, such a recrudescence could be elicited repeatedly during the course of two hours, after which it could no longer be demonstrated.

The same phenomenon has been seen when carbachol was deposited into the hippocampus, as well as in other cortical structures,[31] regardless of whether or not physostigmine was also applied. As illustrated in Figure 10, post-tetanic enhancement of the seizure activity is not prevented

Fig. 9.—Recrudescence of drug-induced changes following an after-discharge (see top two tracings) elicited by electrical stimulation at the same point where acetylcholine and physostigmine had been applied to hippocampus. Left-hand top tracing shows the subsiding drug-induced activity prior to the after-discharge. See text for further details. Calibrations, one second and 200μv.



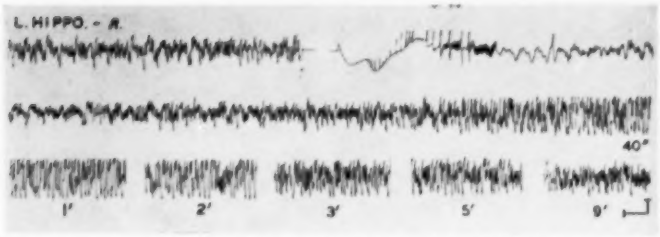


Fig. 10.—Enhancement of carbachol-induced seizure activity following a short hippocampal after-discharge in an animal anesthetized with chloralose and urethan. The after-discharge (following break in top line) was induced by electrical stimulation at the same point where the drug had been applied.

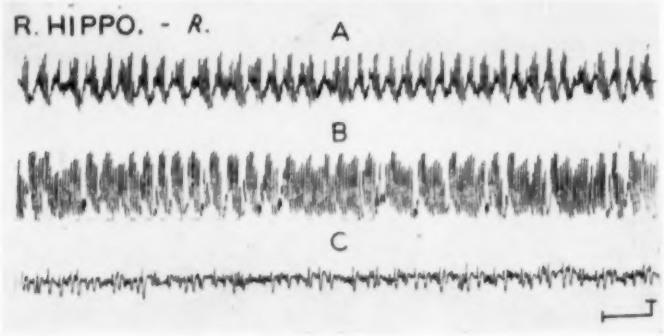
by anesthesia. In this experiment, the animal was anesthetized with chloralose and urethan. Subsequent to the short electrically induced after-discharge shown in the Figure, there was a gradual increase in amplitude of the seizure activity during the next 40 seconds, after which it gradually returned to prestimulation levels during the course of several minutes.

8. *Spontaneous Reactivation During Anesthetization.*—A recrudescence of seizure activity has also been seen to occur spontaneously during the period when an animal is succumbing to an anesthetic dose of pentobarbital sodium. Figure 11*A* shows the abating seizure activity following the deposit of carbachol in the hippocampus of an unrestrained and waking animal. The middle tracing (*B*), showing a recrudescence of the activity, was recorded immediately after the animal fell over after an anesthetic dose of pentobarbital. This recrudescence lasted three minutes, after which the record gradually assumed the appearance of that shown in the bottom tracing (*C*).

III. Propagation of Hippocampal Seizures

To obtain a detailed picture of the cortical spread of electrically and chemically induced hippocampal seizures, the present experiments were performed in acute preparations. Limited exploration was also carried out in subcortical structures. The cerebral cortex of one hemisphere was exposed under ether anesthesia, with the animal in a Horsley-Clarke instrument. Subsequently, local anesthesia was employed, and the animal was maintained under artificial respiration with a quieting dose of tubocurarine U. S. P. or decamethonium (Syncurine). The cerebral cortex was explored with bipolar, ball-tipped stainless steel electrodes placed 2 to 3 mm. apart. Subcortical recording was performed

Fig. 11.—Recrudescence of a carbachol-induced seizure in an animal succumbing to an anesthetic dose of pentobarbital. *A* shows subsiding carbachol-induced activity. *B*, record taken immediately after cat fell down under the influence of the anesthetic. Recrudescence lasted approximately three minutes. *C*, 15 minutes after pentobarbital.



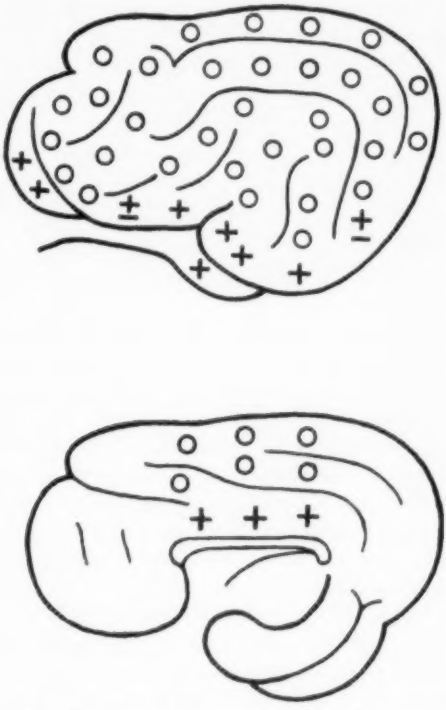


Fig. 12.—Schematic representation of propagation of hippocampal after-discharge to cortex of lateral and medial surfaces of cat's brain, shown respectively in upper and lower drawings: +, clearly positive points; ±, barely detectable propagation; circles, negative points.

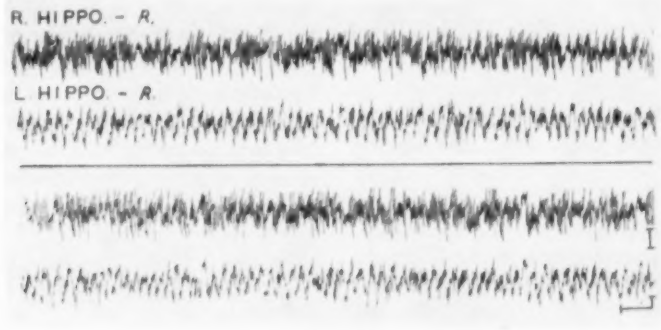
with concentric bipolar electrodes 1.5 to 2 mm. apart.

1. *Electrically Induced Seizures.*—The results of recording the propagation of hippocampal seizures from exposed cortex are diagrammatically represented in Figure 12. They are in keeping with what Kaada [24] and Creutzfeldt and Meyer-Mickeleit [10] found, respectively, in anesthetized and unanesthetized cats.

2. *Chemically Induced Seizures.*—The deposit of carbachol in the hippocampus of the curarized cat failed to elicit as prolonged and sustained high-voltage seizures as in the unrestrained and waking animal. The pattern of propagation was in conformity with that found with electrically induced discharges.

In both acute preparations and unrestrained, waking animals, it has been observed that during the build-up of a carbachol-induced seizure in the hippocampus continuous rhythmic activity, of the type illustrated in Figure 13, appears in the opposite hippocampus. Subsequently, when high-voltage spike potentials develop and are propagated, the rhythmic activity is no longer in evidence. It has also been noted that during the development of carbachol-induced seizures regular activity at 2 to 2.5 per second appears in recordings from the head of the caudate nucleus. As illustrated elsewhere,[38] when the seizure is well developed, corresponding fast potentials of low to moderate voltage may be seen. Other subcortical findings, such as spread to the septal region and hypothalamus, were in keeping with what Creutzfeldt and Meyer-

Fig. 13.—Continuous record illustrating the persisting background rhythmic activity that appears in hippocampus of one side (*L. Hippo.*) at the same time as a carbachol-induced seizure is building up in the opposite hippocampus (*R. Hippo.*) Calibrations, one second and 100μv.



Mickeleit [19] and others have reported in regard to electrically induced hippocampal after-discharges.

Comment

Spread of Chemicals in Brain.—Objections are made to the use of chemical stimulation in the study of functional localization in the brain on the grounds that the injected substances fail to remain localized but spread widely along paths of least resistance or diffuse rapidly to involve remote structures. In the first instance, there is a valid objection when substances are injected in solution. Because of the nonyielding character of brain tissue, even minute amounts of solutions tend to follow paths of least resistance and to escape from the region in which they are deposited. The method used in the present study of depositing chemicals in solid form militates against this complication. The second objection, that chemicals diffuse rapidly and spread widely in the brain, is based on a mistaken assumption. As described in the section on "Methods," it has been shown by the use of dyes and radiophosphorus that cerebral tissue greatly restricts the diffusion of soluble substances. Hyaluronidase fails to increase to any appreciable extent the spread of dyes in the brain. Duran-Reynals interprets such findings as evidence of the relative paucity of ground substance in the brain.[13]

The electroencephalographic and behavioral observations of the present study, as well as of other investigations to be reported, provide further evidence of the slow and relatively localized spread of chemical substances in the brain. Indeed, it early became evident that unless cholinergic agents were deposited in concentrated form there failed to result an activation of sufficient neural elements to bring about significant electroencephalographic and behavioral changes. This finding was surprising in view of the observation by Brink et al. that the application of acetylcholine in high concentration to sympathetic ganglia arrested the activity of nerve cells.[6] In the present experiments is must be inferred that, although the drugs may have arrested neural activity at the point of deposition, they dissolved and diffused out in proper concentration to bring about excitation of large numbers of surrounding neural elements. Presumably, carbachol elicited much more intensive seizure activity than acetylcholine because, not being destroyed by cholinesterase, it continued to spread and excite a greater number of nerve elements.

Variations in Chemically Induced Seizure Patterns.—On the basis of their experimental findings, Chatfield and Purpura have postulated the "existence of two cortical mechanisms, both cholinergic, one of which, the more atropine-sensitive, is inhibitory of the other." [9] Such an hypothesis is appealing in regard to the present study because it may account for the different electroencephalographic patterns elicited by methacholine, on the one hand, and acetylcholine and carbachol, on the other. Methacholine is generally claimed to have a muscarinic action, which is blocked by atropine.[18] This drug did not elicit the spiking activity associated with acetylcholine and carbachol, but produced only an apparent increase in rhythmically recurring potentials. Acetylcholine and carbachol, which have both a muscarinic and a nicotinic action, elicited both rhythmically recurring activity and spiking. Once spiking developed following carbachol, it continued almost without interruption for close to an hour. In one instance acetylcholine also resulted in such uninterrupted firing, but for a shorter time. The postulated inhibitory system of Chatfield and Purpura includes cells of short axon (Golgi Type II cells). In comparison with cortex that differentiates at a later time in phylogeny, the hippocampus is relatively poor in these elements. It is conceivable that an absence of a well-developed "inhibitory system" might account for the "runaway" type of discharge that has been described, a possibility that receives some support from the fact that such prolonged, uninterrupted discharges are not seen in other cortical

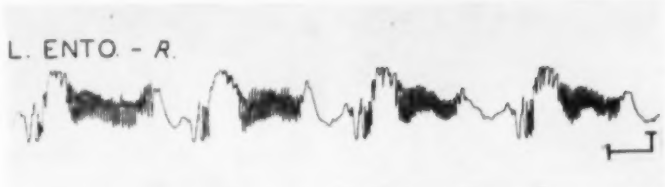


Fig. 14.—Characteristic appearance of seizure activity induced in the posterior hippocampal gyrus (entorhinal cortex) by the deposit of crystalline carbachol. In Figure 5, Line 4, contrast the periodic nature of the above discharge with the uninterrupted seizure activity elicited in the hippocampus by the same drug. Calibrations, 1 second and 200μv.

structures which have a larger number of the elements in question. In the posterior hippocampal gyrus (entorhinal cortex), for example, the drug-induced changes are of the kind illustrated in Figure 14, which shows bursts of potentials followed by relatively silent intervals. The discharges elicited from the hippocampus and entorhinal cortex are so dissimilar as to allow one to tell which of the two structures has been penetrated by the injecting needle.

Although there are individual differences, the configuration of the discharge shown in Figure 14 is generally similar to what one finds in other limbic areas, as well as in the neocortex. No systematic study has been made, but it has significance for the present discussion that in some cortical areas at least methacholine elicits the same type of discharge as is seen with acetylcholine and carbachol. The question of whether or not chemically distinctive inhibitory cells, postulated by Chatfield and Purpura, account for the differences in foregoing seizure patterns is one that possibly can be settled by employing microelectrical techniques.§

In concluding this part of the discussion, it is of interest to point out that as one ascends the phylogenetic scale, one finds an increasing number of cells of short axon in the hippocampus.[48] In observations on rat, cat, and monkey, we have been impressed that in each higher form the voltage necessary to elicit a hippocampal after-discharge becomes greater.

Hippocampal "Injury" and "After-Discharges."—There are various lines of evidence that electrical stimulation of brain tissue results in the liberation of acetylcholine.[51,54] It has been pointed out that the seizure activity induced by carbachol bears many similarities to that of after-discharges elicited by electrical stimulation.[38] The same may be said in regard to "injury" discharges. The possibility therefore suggests itself that both mechanical and electrical stimulation of the hippocampus result in the release of free acetylcholine (or like substance) in an amount that temporarily exceeds the capacity of the local cholinesterase to bring about its destruction.

Recrudescence of Drug-Induced Seizures.

If, as suggested, electrical stimulation results in the release of acetylcholine, it would help to explain the prolonged recrudescence of seizure activity following electrically induced after-discharges in the experiments involving (1) acetylcholine and physostigmine and (2) carbachol alone. In the first instance, it might be inferred that the persistent action of physostigmine at the site of the electrode prevents the local breakdown of acetylcholine released by electrical stimulation. Similarly, carbachol, which has been reported to have an anticholinesterase action (Ammon, cited by Bovet and Bovet-Nitte[4]) might be presumed to act in the foregoing situation like physostigmine. The anticholinesterase action of carbachol in conjunction with the liberation of acetylcholine during light anesthesia[7,11,34] might also

§ This question bears on a number of fundamental neurological problems, such as the variation in the excitability and seizure threshold of various cortical areas, the failure to elicit responses from so-called silent areas, etc.

serve to explain the transitory recrudescence of carbachol-induced seizures that is seen in an animal succumbing to an anesthetic dose of pentobarbital.

Hippocampal Rhythmic Activity.—Electrophysiological studies have shown that stimulation by way of various intero- and exteroceptive systems results in rhythmically recurring potentials in the hippocampus.[19,22,30,41] Slow regular activity occurs spontaneously when an animal is aroused or alerted or appears to shift or focus its attention.[19,30] Green and Arduini have found that electrical stimulation of the midbrain tegmentum, hypothalamus, preoptic region, septum, and intralaminar nuclei evokes comparable changes.[19] In this laboratory it has been found that continuous rhythmic activity may be recorded from the hippocampus for prolonged periods following the deposit of cholinergic drugs not only in the contralateral hippocampus, as reported above, but also in the septal nuclei, hypothalamus, periaqueductal region, and ventricular system.

In all the foregoing instances it may be inferred that the rhythmic activity is engendered by extrinsic neural influences. The present study has shown that slow rhythmic activity can also be induced by the local application of cholinergic agents to the hippocampus. The elements that give rise to this activity are unknown. But whatever its source, there is evidence, under certain circumstances, of a correlation between the waxing and the waning of these slow potentials and the excitability of some of the neural elements. This was illustrated in Figures 5 and 6, which show that during the development and subsidence of carbachol-induced seizures fast oscillatory or spiking potentials tend to group themselves near the peak and on the falling phase of the slow potentials. In a study using microelectrodes, Green and Machne reported that in some instances "slow hippocampal rhythms following a seizure discharge induced by stimulation of the hippocampus of the opposite side were seen to have a very exact correspondence with bursts of unit discharges."[20] A similar relationship was occasionally seen during resting activity and following some forms of sensory stimulation.

Long-continued rhythmic activity has been observed in the hippocampus during certain stages of ether anesthesia and following the administration of reserpine.[42] It is unknown whether this activity is primarily attributable to a local action of these agents on the hippocampus or to their effect on related structures, but it is of interest to point out in regard to what has just been said that light ether anesthesia results in the liberation of acetylcholine in the brain.[7,34] Whether or not reserpine acts similarly deserves investigation.

With continued investigation in this laboratory, it has become evident that the entire hippocampus does not show uniformity in regard to the rhythmic activity under consideration. The portion proximal to the amygdala appears to manifest random fast activity in most of the situations that have been mentioned. In this regard, its behavior is comparable to that of the cortex of the outer convexity of the brain. There is no ready anatomical or physiological explanation for these discrepancies.

Propagation of Hippocampal Seizures.—The significance of the findings of this aspect of the study will be discussed in Part II of this study.

Summary

This study represents one of a series of investigations on the functions of parts of the hippocampus and other structures of the limbic system. The present experiments were performed on cats and focused attention on an intermediate segment of the hippocampus lying between frontal planes A1.5 and A4.5 of Horsley-Clarke coordinates.

Reasons are given for employing "cholinergic" as well as electrical stimulation in this particular study. A method is described that allows one to stimulate electrically or chemically the same point in the brain and at

the same time to record the electroencephalographic and behavioral changes in unrestrained animals. In addition to the technical procedure, this communication deals with the electroencephalographic findings. The following paper will report the behavioral observations.

Primary consideration is given to the electroencephalographic changes following the application of acetylcholine (with physostigmine) methacholine, and carbachol. Application of these agents in crystalline form militates against their escape from the region in which they are applied and thereby helps to circumvent a complication that occurs with the use of solutions. Such application also provides the most effective means of eliciting pronounced and enduring electroencephalographic changes. Evidence is presented that cerebral tissue greatly restricts the spread of soluble substances in the brain.

The most pronounced EEG changes are seen with carbachol. Two to four minutes after its application rhythmic potentials at about 20 per second appear and are frequently grouped in the form of spindles. Subsequently they increase in amplitude and may occur in long trains. Intermittently background slow rhythmic activity is seen, and at such times the fast potentials tend to group themselves near the peak and on the falling phase of the slow waves. Seven to fifteen minutes after the drug is deposited, high-voltage spikes begin to appear interspersed among the fast oscillatory potentials. Subsequently they may occur almost continuously for periods of 45 to 60 minutes, reaching amplitudes of 1400μv to 1600μv. After this prolonged discharge, the seizure gradually subsides during the next hour or two, dissipating in the same patterns of activity that characterized its development. As it dies out, slow rhythmic activity becomes the conspicuous feature of the record.

The changes occurring with acetylcholine are in many ways similar to those seen with carbachol, but are much less intense and shorter in duration, seldom lasting more than an hour. Unless acetylcholine is used in conjunction with physostigmine, pronounced and enduring changes are not consistently obtained.

The application of methacholine is characteristically followed by the appearance of persisting slow rhythmic activity with superimposed fast potentials. In the hippocampus this agent does not elicit the spike potentials seen with the former two drugs. A possible explanation of the difference in the respective seizure patterns is discussed.

When seizure activity is beginning to subside after the application of (1) acetylcholine and physostigmine or (2) carbachol alone, it shows a prolonged recrudescence following an after-discharge elicited by electrical stimulation at the point where the chemicals were applied. A recrudescence also occurs spontaneously when an animal is succumbing to an anesthetic dose of pentobarbital. Possible explanations for these phenomena are considered.

Attention is drawn to the similarity between the seizure activity induced by carbachol and that associated with injury discharges and electrically induced after-discharges. The possibility is suggested that injury and electrical stimulation result in a release of acetylcholine in an amount that temporarily exceeds the capacity of the local cholinesterase to bring about its destruction.

An investigation on the propagation of electrically and chemically induced hippocampal seizures to other cerebral structures is described.

The slow rhythmic activity that occurs in the hippocampus of waking animals under a variety of conditions is discussed in the light of the present experiments.

References are given at the end of Part II.

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Chemical and Electrical Stimulation of Hippocampus in Unrestrained Animals

II. Behavioral Findings

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The present study represents one of a series of investigations on the localization of function in the limbic system and deals with the results of electrical and chemical stimulation of an intermediate segment of the hippocampus in the cat, the limits of which were stated in Part I. On the basis of anatomical information, it is probable that this segment receives overlapping afferents from the angular bundle and the cingulum.[32, 49] A major portion of the fibers of the angular bundle are from the posterior part of the hippocampal gyrus (entorhinal area of Brodmann, angular ganglion of Cajal). There is evidence that the cingulate cortex contributes to the large bundle of fibers in the cingulum.[49] The foregoing anatomical findings are supported by studies employing strychnine neuronography.[47] Furthermore, it appears evident from such studies[47] that the part of the hippocampus under consideration, in contrast to the portion lying proximal to the amygdala, is not fired by the frontotemporal cortex of the limbic system (posterior orbital, insular, temporal polar, and pyriform cortex).

Initial exploration with electrical stimulation indicated that the portion of the hippocampus under study was relatively "silent." As explained in Part I, the possibility suggested itself that prolonged cholinergic stimulation might bring about changes that could not be demonstrated in the foregoing manner. A method was therefore devised which allows one to compare the effects of chemical and electrical stimulation of the same point in the brain and at the same time record the electroencephalographic changes in the unrestrained and waking animal. Part I described this method and the experimental procedure and reported the electroencephalographic observations. The present paper will deal with the behavioral findings.

Materials and Methods

The reader is referred to Part I for a description of methods and procedures. Most of the chemical stimulations involved the use of acetylcholine (with physostigmine), methacholine (Mecholyl), and carbachol (Doryl). Behavioral observations were made on 28 cats. Simultaneous EEG recordings were obtained in 18. Toward the end of this study construction was completed on a special viewing stage designed for conditioning experiments and making motion pictures. This stage, built in the form of an arc and having a concave window of hard-surface Lucite, allowed pictures to be obtained with a constant lighting source and with the animal kept within the focal range of the camera. Films documenting the findings to be reported here have since been obtained in the course of collaborative investigations dealing with specific behavioral alterations following chemical and electrical stimulation of the hippocampus. The illustrations used in this paper are from motion pictures taken during experiments performed in collaboration with Drs. Chul Kim and John Flynn. To provide supporting evidence of a comparative nature, a brief description will be given of behavioral changes in the rat during and

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following hippocampal seizures. These observations were made in the course of an endocrinological study performed in collaboration with Dr. Alvin Brodish.

Terminology.—As frequent reference will be made to enhanced pleasure and grooming reactions and to receptivity to genital manipulation, a statement will be made as to the meaning of these expressions. Enhanced pleasure reactions will refer to the appearance in a conspicuous form of those manifestations that are interpreted as signs of contentment and passivity in the cat. These include spontaneous loud purring; kneading and fanning of forepaws; turning over on back, rolling, twisting, stretching, and fanning of forepaws; rubbing head and body vigorously against inanimate objects or the examiner. Enhanced grooming will refer to the appearance in a conspicuous and enduring form of grooming activity. Receptivity to genital manipulation, over and above its manifest meaning, will imply the susceptibility of the male cat to the inducement of penile erection. In our own experience and in the experience of others it is only a rare male cat that will not resist and avoid genital manipulation. For example, Root and Bard state: "In the normal male cat it proved impossible, except immediately after the subsidence of an erection accompanying sexual activity, to evoke any degree of penile turgidity by manipulation of the organ. Such a procedure almost always induced vigorous signs of anger."[22]

Results

I. Chemical Stimulation of the Hippocampus

The following account is based on observations on 18 cats in which simultaneous electroencephalographic recordings afforded the opportunity to ascertain the presence or absence of drug-induced changes in the hippocampus. The sites of the needle electrodes are schematically shown in Figure 2 of Part I. Crystalline acetylcholine was deposited in the hippocampus on nine occasions; methacholine, eight times, and carbachol, eight times. It is to be noted that this numeration excludes injections into the fimbria. The drugs were applied in amounts usually ranging from 0.03 to 0.06 cu. mm. In the case of methacholine and carbachol, the tip of the injecting needle was sealed with physostigmine or sugar. With acetylcholine, physostigmine was used on all but one occasion.

1. *Immediate Sequelae.*—There were a number of behavioral manifestations that occurred variably and sporadically at the time the injecting needle induced the injury discharge in the hippocampus or during the subsequent five minutes. These included meowing; sniffing and looking upward; retraction of ipsilateral ear; contractions of ipsilateral face; tendency to closure of the ipsilateral eye and relaxation of nictitating membrane; licking; slight salivation; mydriasis, and defecation and urination. Sometimes there was moderate cardiac acceleration during the injury discharge.

2. *Acetylcholine and Methacholine.*—Except for an apparent enhancement of pleasure and grooming reactions following 9 of 17 stimulations, there were no significant behavioral manifestations that could be correlated with the bioelectrical changes induced by these drugs. It is to be emphasized that these changes in disposition were in striking contrast to the angry behavior that resulted if these drugs were injected into the hippocampus in solution and escaped into the overlying ventricle (see below). They gain added significance in the light of the following two experiments: At one time, owing to a shortage of cats, it was decided to use two animals that had been set aside for acute experiments under anesthesia because they were of such a mean disposition. During a month of observation they had at no time been observed to show friendly behavior but, on the contrary, would hiss, spit, and assume an angry, defensive attitude whenever approached. It was, therefore, striking to find that both spontaneous and induced pleasure reactions first occurred in these animals when changes resulting from chemical stimulation appeared in the EEG. The fifth line of Figure 4 of Part I illustrates the nature of the drug-induced activity in the hippocampus of one of these animals at the time pleasure reactions first became evident.

3. *Carbachol.*—The behavioral manifestations following carbachol were found to correlate with three stages of electroenceph-

alographic changes: (1) stage of development; (2) stage of culmination, and (3) stage of subsidence.

(1) Stage of Development: During the first 15 minutes, with the build-up of seizure activity, there is little forewarning of the profound behavioral changes found in the second stage. The cat may appear as though settling down to sleep, or it may occasionally manifest some sniffling and furtive looking about and upward. It appears to respond appropriately to external stimuli.

(2) Stage of Culmination: About 15 minutes after carbachol, high-voltage spiking activity becomes practically continuous in the hippocampus (Line 4 of Fig. 5, Part I), and concurrently the cat lapses into a state in which it appears to be in a stupor. It shows a lack of spontaneity of movement and seems oblivious to incidental noises and commotion in the environment. The absence for the most part of convulsive activity in the body musculature stands in striking contrast to the intense nature of the seizure recorded electrically. Two animals showed some ipsilateral convulsive movements of the face.

The apparent loss in psychic capacities, as opposed to the retention of postural, locomotor, and viscerosomatic reflexes, can be illustrated by the animal's behavior during a number of manipulations. Although the pupils react to a light, the animal will not avoid the light, nor will it cringe when one pretends to strike the face. One may continually blow smoke into its face and there will be blinking and tearing of the eyes, but the animal will not move away. The head may shrink back momentarily but will return just as quickly to the source of irritation. In general, there appears to be underreactivity to all forms of noxious stimuli of moderate intensity. Intense noxious stimulation, however, results in behavioral changes that are remarkably dramatic because of their violence and the suddenness of their onset and termination. If the cat's nose is momentarily touched with a hot object, the animal may suddenly jump a distance of several feet and then just as suddenly assume a pseudocatatonic stance that will be maintained for a minute or more. A momentary hard pinch of the tail may cause the animal to dart suddenly forward for several steps, after which it will abruptly stop in a trance-like state. If such a pinch is continued, the cat will growl, hiss, strike out, and thrash about in a frenzy, or bite at a food dish or any object immediately in front of it. It seems utterly confused and blind as to the source of the stimulus. As a consequence, one can give a prolonged hard pinch to the ear with complete impunity. During the period of frenzy there are pupillary dilatation, salivation, and marked cardiac acceleration. Upon cessation of the noxious stimulus, the animal suddenly assumes a prolonged catatonic-like stance. In the meantime, salivation ceases, the pupils return to their former size, and the heart rate falls to within normal limits.

In regard to the catatonic-like manifestations, it is to be noted that sometimes the animal may be draped into various postures, which it will maintain for minutes at a time. This is illustrated by Figure 1, which shows a cat placed in a sitting posture with one forepaw elevated and resting awkwardly on a stool. Unlike the cataleptic state, however, there is no perceptible increase in muscle tone. The animal's ability on provocation to run and jump without falling attests to the retention of righting mechanisms. There is the additional significant finding that the cat may be dropped upside down from a height and right itself.

During the height of the seizure, unless one stimulates the animal into action, the heart and respiratory rates do not show an appreciable change from the values observed prior to the application of carbachol. In two instances stroking the genital was noted to result in a forceful evacuation of urine without the animal's assumption of appropriate posture.

(3) Stage of Subsidence: During the second and third hour, when the seizure activity is abating, the cat may manifest

Fig. 1.—An excerpt from motion pictures illustrates that during Stage 2 of a carbachol-induced hippocampal seizure an animal may be placed in awkward postures which it will maintain for minutes at a time.

enhanced pleasure and grooming reactions and be unusually receptive to genital manipulation. One animal embraced the arm of the experimenter in a sloth-like manner and could thus be suspended in the air during genital stimulation. Over and above the oral activity associated with grooming, the animal may engage in prolonged gentle biting and licking of the hand of the experimenter.

Fig. 2.—If the high-voltage seizure activity associated with Stage 2 of a carbachol-induced hippocampal seizure fails to develop, an animal may show only unusual receptivity to genital stimulation and the enhanced pleasure and grooming reactions that characterize Stage 3. This illustration from moving pictures shows an induced, sustained erection in such an animal.

If insufficient carbachol is deposited in the hippocampus to induce high-voltage seizure activity and the associated behavioral changes seen in Stage 2 (see above), the only noteworthy findings are enhanced pleasure and grooming reactions and receptivity to genital stimulation. Figure 2 shows an induced, sustained erection in such an animal.

In the event that the needle makes a shallow penetration of the hippocampus and the drug escapes into the ventricle, the animal manifests contralateral circling and angry behavior of the type to be described below in giving the results of intraventricular injections of cholinergic agents. If, at the same time, high-voltage seizure activity builds up in the hippocampus, the animal is unable to direct its angry behavior.

4. *Other Drugs.*—In one instance potassium penicillin G was deposited in the hippocampus. This agent elicited randomly recurring negative spikes, which during the first half-hour occurred as frequently as 1 per second and reached an amplitude of 700μv (Fig. 8, Part 1). After the appearance of the spikes, the animal groomed intensively and continuously for a period of 18 minutes, particularly in the region of the groin and genitals. The movement artifact

appearing in the EEG recording throughout this period provided a graphic measure of the grooming activity.

In preliminary studies prior to making electroencephalographic recordings, a variety of drugs were injected into the hippocampus to ascertain whether or not they would induce significant behavioral changes. These included epinephrine, arterenol, pilocarpine, tubocurarine, strychnine, and pentylenetetrazol U. S. P. (Metrazol). As the results did not appear to be promising, further investigation was not carried out.

5. *Incidence of Enhanced Pleasure and Grooming Reactions.*—A review of the protocols disclosed that enhanced pleasure and grooming reactions were observed following 14 of 26 chemical stimulations of the hippocampus and involved 10 of the 18 animals. This observation compared with 2 such positive reactions following 28 chemical stimulations elsewhere, including 7 in the fimbria, where in no instance were EEG changes observed. These reactions were not noted on eight occasions when empty needles or sucrose was placed in the hippocampus.

II. Effects of Intraventricular Injection of Cholinergic Drugs

In preliminary experiments, when the hippocampus was injected with 0.01 cc. of 10% acetylcholine and an equal amount of 0.5% physostigmine, or with 2.5% methacholine (with or without physostigmine), there resulted a characteristic syndrome in which the animal circled to the contralateral side and displayed angry behavior. In addition to the finding that such injections are complicated by the leaking back of the solution along the needle into the ventricle ("Materials and Methods," Part I), there are the following reasons for attributing the foregoing syndrome to stimulation of other structures lining the ventricular system. The same manifestations could be obtained by injecting directly into the lateral ventricle above the caudate nucleus, and angry behavior without contralateral circling was associated with injections into the third ventricle or surrounding gray matter close to the aqueduct.

The onset of the syndrome was usually signaled by barely audible growling three to four minutes after the injection, often occurring with every other breath. Shortly after, the animal would commence to circle intermittently to the opposite side, and at the same time the growling became louder and was periodically punctuated with hisses. Any external stimulus characteristically evoked hissing and circling. Sometimes there would be frenzied circling for as long as 10 minutes. If an injection was then made on the other side, circling occurred in the opposite direction.

The spontaneous hissing and growling were associated with furtive looking that suggested a preoccupation with some hallucinatory experience. Sometimes an animal would make a ferocious, directed attack if approached. The attack usually could not be directed if one approached from the side of the injection. There seemed to be an inability to orient to any stimulus (e.g., sound, touch) that came from that direction; almost invariably the head turned toward the opposite side. The angry manifestations gradually subsided during the course of an hour, after which the animal was usually receptive to petting.

In subsequent experiments involving the deposit of crystalline carbachol, it was found that the same syndrome occurred if the drug entered the ventricular system. The symptoms, however, were generally more intense and longer in duration. Angry behavior might persist for as long as seven hours. Although the animals would readily attack any person who approached them, they would no more than hiss or growl at a rat or a mouse. In these experiments, fine tremors of the head were sometimes so pronounced as to interfere with recording the EEG.

In all the foregoing experiments, there was a variety of autonomic manifestations. In cases in which electrocardiographic trac-

ings were obtained, there was found a marked cardiac acceleration during the period of angry manifestations, e. g., from 120 to 240 beats per minute. Pupillary dilatation was a common finding. In the protocols of 18 experiments, salivation was noted to be pronounced in 6 instances, piloerection in 5, "shivering" in 5, and panting in 4. In one animal showing panting after carbachol, the respirations continued at a rate of 200 per minute for over a period of two hours. Urination was noted but two times and defecation once. Sweating of toe pads was not observed in any animal.

Comment.—Sherwood et al. reported angry "hallucinatory" behavior in cats in association with intraventricular injections of acetylcholine and related compounds.[56] Apparently it was not so marked as that described here. They did not comment on contralateral circling. On the basis of experiments to be described elsewhere, it is probable that the contralateral circling can be attributed to stimulation of the caudate nucleus.[57] Such circling has been a common finding following cholinergic stimulation of this nucleus, but not of other structures lining the ventricular system, specifically the hippocampus, dorsal thalamus, septal nuclei, and hypothalamus. Other evidence indicates that the angry behavior and autonomic manifestations are the result of activation of gray matter surrounding the third ventricle and the aqueduct. In one animal, when carbachol was deposited in the gray matter close to the aqueduct, angry manifestations persisted until the time the animal was killed, three days later. In contrast to injections in the lateral ventricle, those involving the third ventricle and surrounding gray matter result in angry behavior that is readily prosecuted in any direction.

III. Behavioral Changes During Electrical Stimulations of Fimbria and Hippocampus

Electrical stimulation was usually carried out after the drug-induced electroencephalographic changes had disappeared or practically subsided. In nine instances empty needles were inserted for the purpose of recording and stimulating. The sites of the electrodes are indicated in Figure 2, Part I. Various parameters of stimulation were used. The following account is based on results obtained when the stimulator was set to deliver 1 msec. pulses at 60 per second. Stimulation was usually applied for not longer than 10 seconds. The responses seen during stimulations at 37 electrode positions with a stimulus intensity below or at just threshold for eliciting an after-discharge are tabulated in the accompanying Table. The number of times a particular response was obtained by stimulating points within plus or minus 1 mm. of the frontal planes shown in Figure 2*A* and *B* of Part I, respectively, are listed in the first two columns. The third column gives totals.

It is apparent from the Table that the hippocampus at plane A2 was relatively "silent" as compared with plane 4, where the electrodes were frequently in a position to contact the fimbria. The animal's turning of the head, the commonest finding, frequently suggested an attitude of alerting and attentiveness, particularly if accompanied by a pricking of the ears and some pupillary dilatation. There were the following additional observations: Purring, if already present, continued throughout the period of stimulation. With strong intensities of stimulation, an occasional animal might momentarily growl or hiss or jump, or suddenly circle in a direction away from the side of stimulation.[25]

Responses to Electrical Stimulation of Hippocampus and Fimbria

	Frontal Plane A2 (±1 mm.)*	Frontal Plane A4 (±<1 mm.)†	Total
Number of electrode positions	22	15	37
No response	15	4	19
Contraversion of head	5	9	14
Ipsilateral closure of eye	2	8	10
Dilatation of pupils	2	5	7
Pricking of ears	0	3	3
Cringing away from stimulated side	1	2	3
Ipsilateral retraction of ear	0	3	3
Wrinkling of ipsilateral face	0	2	2
Meowing	0	1	1

* See Figure 2*A*, Part I.
† See Figure 2*B*, Part I.

IV. Behavior During Hippocampal After-Discharges

Hippocampal after-discharges were elicited with potentials that were usually zero to ½ volt greater than those required to elicit a behavioral response. In the majority of instances they developed within 10 seconds of stimulation with the stimulator set at 2-3 volts (other parameters as above) and lasted on the average of 22-23 seconds. The amplitude of the discharge generally ranged from 500μv to 1000μv. In keeping with the descriptions of Rosenblueth and Cannon [53] and others,[2,30] there was great variation in the configuration of the discharge. It usually began with trains of potentials at 6-8 per second that subsequently increased in frequency to 25-30 per second, but the reverse picture was also seen. The frequency of the potentials characteristically slowed when silent intervals began to appear toward the end of the discharge.

A description of the behavioral changes during hippocampal after-discharges has been given in previous communications [38-40] and will not be repeated in every detail. Except for the incipient and terminal manifestations, the changes that occur spontaneously or that can be induced during the after-discharge are in almost every way similar to those that have already been described in regard to carbachol-induced seizures. Dilatation of the pupils is a common indication of the beginning of the discharge. Purring, if previously present, may cease and be replaced by occasional meows or yowls. Any turning movements that were present during the period of stimulation appear to reverse themselves with the onset of the discharge, and the animal assumes a facial expression and bodily attitude that often suggests fearful alerting or rapt attention. This state of apparent readiness for action stands in striking contrast to its inability to respond appropriately to happenings in the environment. As in the case of carbachol seizures, there is usually underreactivity to noxious stimuli of moderate intensity, although occasionally angry behavior will occur explosively on the slightest provocation. The manifestations elicited by intense noxious stimulation are similar to those described in regard to carbachol. There is typically an inability to give direction to induced angry behavior. When the tail is pinched, the cat may dig its teeth into any object immediately in front of it or turn and bite at the stump of its tail. Upon cessation of the noxious stimulus, it suddenly assumes a catatonic-like stance, in which it appears to be in a trance.

V. Behavior Following Hippocampal After-Discharges

The end of the after-discharge is usually signaled by a meow or yowl, after which there may be intermittently a series of such vocalizations. The animal's demeanor during this time is variously suggestive of a state of bewilderment, confusion, questioning, or, rarely, panicky excitement.

The rest of this account is broadly descriptive of the enhanced pleasure and grooming reactions that were seen in 9 of 15 animals following hippocampal after-discharges. As soon as vocalization ceases, the animal starts to scratch its head or body or begins to lick and bite near the stump of the tail or in the genital region. Afterward there may follow a period of protracted intensive grooming. The grooming may, from the start, be largely confined to the genital region, or may involve an orderly progression from head and forepaws, to body and hindlimbs, to stump of tail and region of anus and genitalia. In the male a partial erection may appear in the course of protracted licking of the genitalia. This occurred in the cat shown licking its genitals in Figure 3. Intensive grooming activity may continue for as long as five minutes, after which the animal may stretch out, purr, fan its forepaws, and show other manifestations of contentment. If approached by the experimenter during the period of grooming, the animal characteristically manifests enhanced pleasure reactions.

Fig. 3.—Following electrically induced hippocampal after-discharges both cats and rats commonly engage in extensive grooming. The grooming may involve all parts of the body or focus from the start on the genital region. During grooming of the genital region partial penile erections may be seen. Such was the case of the cat shown in the cinematographic excerpt above.

VI. Note on Hippocampal Recording and Stimulation in Rat

These experiments are pertinent from a comparative point of view to the grooming behavior that has just been described. Electrodes for recording and stimulation were placed in the segment of the hippocampus proximal to the fornix in nine rats. Experimentation was carried out with the animals in their own cages. The hippocampogram showed random fast activity of low to moderate voltage intermixed with regular activity around 6 per second and with voltages up to 300μv. The regular activity characteristically appeared when an animal seemed to focus its attention or was exploring, and disappeared when it was eating or drinking. Electrical stimulation with voltages that failed to elicit after-discharges did not elicit any consistent responses. Sometimes an animal would begin to sniff and explore. After-discharges were elicited with potentials of less than 1 volt. During the after-discharge, the animal would frequently become motionless and assume a prolonged statuesque posture while sitting on its haunches. Sometimes it would shake itself violently, like an animal that had received a wetting. Following the after-discharge the animal characteristically became very actively engaged in grooming and frequently would shake itself violently in the manner just described. One might see a partially erected penis when the grooming focused on the genital region. The intensive grooming activity and shaking commonly lasted for periods up to five minutes following an after-discharge. In a few instances, prolonged drinking of water was noted. One animal was observed to drink for 3 minutes and 20 seconds.

Comment

Hippocampal Seizures.—Behavioral observations have been made upon rat[40] (see above), guinea pig,[8,30] cat,[2,8,38,40] monkey,[1,42] and man[46] during hippocampal seizures. Although varying interpretations have been placed on the behavioral changes during such seizures, all observers appear to agree that there is a loss to some extent of what may be descriptively referred to as "awareness." The deficit in this regard impresses itself much more forcefully on one when observing an animal during prolonged carbachol-induced seizures than during short-lasting hippocampal after-discharges. In order to obtain some measure of the psychological impairment during hippocampal seizure, we have been conducting a series of studies employing conditioning methods. The first group of experiments tested the effect of carbachol-induced seizures on the behavior of animals (cat and squirrel monkey)

trained in a shuttle box to avoid a shock following the sound of a buzzer.[42] It was found that at the height of the seizure the animals failed to respond to the conditioned stimulus, and also sometimes failed upon receiving the unconditioned stimulus. It has since been found that electrically induced propagating hippocampal after-discharges have a parallel effect. They also abolish or markedly alter conditioned cardiac and respiratory responses.[42]

There remains uncertainty as to how extensively a hippocampal seizure must spread before there is a perceptible change in an animal's "awareness." One obtains the impression from some descriptions that this alteration depends on the propagation of the discharge to the primary projection areas [1] or to the "association cortex" of the lateral convexity.[2,25] We have repeatedly found in the conditioning studies referred to above that a loss of conditioned responses occurs without such a spread. Moreover, when clicks were used as the conditioned stimulus, they evoked potentials in the auditory areas during the after-discharge just as they did before. It appears, however, that with poor propagation of the discharge to the contralateral limbic structures there may be either no or only partial interference with the conditioned response.

Inconsistencies that are found in reports on the spread of hippocampal after-discharges can be attributed to a number of variables. One factor of major importance pertains to the vagaries of volume conduction. Because of the very high voltages of the propagating hippocampal after-discharges, they may manifest themselves in remote regions because of volume conduction. In the acute experiments reported in Part I, in which experimentation was carried out with direct exposure of the cortex, it was found that an after-discharge could be readily recorded from the outer convexity if there was wide spacing between the electrodes or if one electrode was so placed as to be relatively indifferent. Such situations might account for the finding of widespread propagation to the outer convexity in a chronic experiment in which electrodes were too widely placed or in which one electrode rested on the brain and the other on the dura. Figure 12 of Part I shows the extent of cortical propagation that was found when moderate stimulus intensities were used to induce an after-discharge and when the cortical potentials were recorded with bipolar electrodes spaced 2 to 3 mm. apart. The findings are in keeping with those reported by Kaada [24] and Creutzfeldt and Meyer-Mickeleit.[10]

Andy and Akert have observed that during hippocampal seizures noxious stimuli evoke well-organized defense reactions in the cat.[2] Our findings are in agreement with this, and in addition we have emphasized in this and in previous communications [38-40] that during both drug- and electrically induced seizures the animal usually appears unable to direct its attack. We have seen a like impairment in the squirrel monkey. In subsequent experiments with multiple electrode placements we have found that the cat's inability to direct angry attack does not depend on a spread of the discharge to the cortex of the lateral convexity. Contrary to the findings of Andy and Akert and ourselves, Cadihlac [8] reports that during hippocampal seizures sparing the *cortex et la reticulée* the cat is in such a profound state of catalepsy that it is unable to be aroused by violent and painful stimuli. There is no doubt that such is sometimes the case, but it is our impression that in the majority of instances the cataleptic state can be changed into one of "sham rage" by intense noxious stimulation, only to reappear suddenly again when such stimulation is terminated.

Bard and Mountcastle have reported that bilateral ablation of the hippocampus in the cat results in an increase in the threshold required to evoke signs of rage behavior.[3] Brady and Hunt have noted that rats following such ablations show signs of anger when the tail is pinched but appear unable to direct their attack.[5] The latter observa-

tions are reminiscent of the behavior of animals during propagating hippocampal seizures and are compatible with a suggestion made elsewhere that such seizures, being largely confined to limbic and perilimbic structures, result in what must amount, in part, to a "functional ablation" of the limbic system.[10,42]

The significance of studies on hippocampal seizures in regard to the pathophysiology of psychomotor epilepsy, as well as to psychotic catatonic manifestations, has been considered in other papers and does not need to be reelaborated upon here.[38-40] Certain relevancies of this problem to gaining insight into the mechanism of action of reserpine have also been discussed elsewhere.[42]

Electrical versus Chemical Stimulation.—In regard to responses during electrical stimulation, it was observed that the caudal part of the hippocampal segment under study was relatively "silent" as compared with the rostral portion (Table). In the rostral portion, the electrodes were frequently in a position to contact the fimbria, and it is possible that some of the defensive attitudes evoked by stimulation were the result of activating fibers from the part of the hippocampus proximal to the amygdala, where, as previously reported,[37] stimulation may result in such responses, as well as other self-protective manifestations. Except for two instances during the height of carbachol-induced seizures when there were ipsilateral convulsive movements of the face, cholinergic stimulation, which ostensibly does not activate nerve fibers, did not evoke any of the motor manifestations listed in the Table.

Enhanced Pleasure and Grooming Reactions.—These reactions following chemical and electrical stimulation were briefly described in previous communications.[38-40a] Recently Cadihlac has made passing comment on augmented pleasure reactions following hippocampal seizures in the cat.[8]

Perhaps the greatest contribution of chemical stimulation in these studies was to direct the attention of the experimenter to the possible significance of enhanced pleasure and grooming reactions following the induction of neuronal discharge in the hippocampus. As already noted, these reactions were in marked contrast to the angry behavior that occurred if the cholinergic drugs escaped from the hippocampus into the overlying ventricle. In the early experiments these reactions were not specifically looked for. They were at first recorded in the protocols either because they seemed to provide evidence that the stimulations had no effect or because, in making it difficult to obtain electroencephalograms free of artifact, they forced themselves on the attention of the experimenter. The subsequent finding that these animals were unusually receptive to genital stimulation, and that in the male cat sustained erections could be induced, attracted further attention to their possible significance. Finally, when it was observed that such behavior commonly occurred in cats following electrically induced hippocampal seizures, and that enhanced grooming behavior with occasional penile erection occurred in similar circumstances in the rat, it began to seem unlikely that the findings were spurious in nature. It is also noteworthy in this regard that in a single instance in which carbachol was introduced in the hippocampus of a squirrel monkey (not reported above) a spontaneous partial erection developed 13 minutes after the onset of the seizure.

Enhanced pleasure and grooming reactions were made note of in the protocols of 10 of the 18 animals in which electroencephalographic recordings were obtained and followed 14 of 26 chemical stimulations. This observation compared with 2 such positive reactions following 28 chemical stimulations elsewhere, including 7 in the fimbria, where in no instance were EEG changes observed. These reactions were not seen on eight occasions when empty needles or sucrose was placed in the hippocampus. If

* See also discussion following abstract of paper by MacLean.[39]

these results were subjected to χ^2 analysis, they would be highly significant ($P<0.001$).

There are, however, obvious reasons why an exploratory study of this kind is not suitable for formal analysis. But even in a study in which the presence or absence of the foregoing responses was specifically looked for from the beginning, and in which there was a number of independent observers,† there would still remain the difficulty of assessing the significance of what has been defined as enhanced pleasure reactions and establishing their relationship to brain stimulation. Grooming behavior lends itself to more objectivity. In addition to having a typical motor pattern, its presence and duration are graphically recorded in the electroencephalogram by the typical artifacts caused by the animal's licking and scratching. In this laboratory, Dr. Chul Kim has made an independent analysis of the incidence of grooming following electrically induced hippocampal after-discharges in 19 animals.[28] (These experiments did not involve chemical stimulation.) The knowledge was kept from him that pleasure and grooming reactions occurred in 9 out of 15 animals in the present experiments following such discharges, an incidence of 60%. He observed grooming following after-discharge in 12 of the 19 animals, an incidence of 63%. The similarity of the findings is highly suggestive of a significant relationship of the grooming phenomenon to the after-discharge.‡

As will be indicated shortly, continuing investigation is beginning to suggest that a neural system involving the hippocampus, cingulate gyrus, and septum is implicated in the pleasure and grooming reactions and the sexual manifestations that have been close anatomical relationship of these strucdescribed. Long ago Cajal described the tures.[49] He concluded that "physiologically, the septum should be considered a nerve center associated with or subordinate to Ammon's horn and the fascia dentata." Recent anatomical [12] and physiological [19] studies have added significant details in regard to an afferent supply to the hippocampus through the septum and fornix. The medial septal nuclei appear to be one source of such connections.[12] In this laboratory, Trembly observed enhanced pleasure reaction in cats following 8 of 11 cholinergic stimulations of the medial septal nuclei.[58] Such responses were not seen following an equal number of stimulations elsewhere in the septal region. Kim observed pleasure reaction following after-discharges elicited by electrical stimulaton of the septum and in one instance noted a spontaneous penile erection.[26] He has also seen spontaneous erections following electrical or chemical stimulation of the anterior supracallossal cingulate gyrus. Spontaneous or easily induced erections have been observed in a few instances by Lockhart [31,38,39] during seizure activity induced by the application of cholinergic drugs to the cortex just above the posterior cingulate gyrus.§ In 1909 von Bechterew reported that his collaborator, L. Pussep, elicited penile erection in the dog upon stimulation in the region of the anterior thalamus.[59] These stimulations might have involved the anterior thalamic nuclei, which are anatomically related to the cingu-

† Whenever there were incidental observers of the present experiments, their impression regarding enhanced pleasure and grooming reactions concurred with the experimenter's.

‡ Once post-after-discharge grooming has been demonstrated in an animal, it can be elicited on subsequent stimulation and on different days with a fair degree of predictability. For example, I scheduled a class demonstration to illustrate the various changes that occur during and following hippocampal after-discharges. At the demonstration the animal showed all the manifestations that have been dealt with in this discussion: loss of conditioned avoidance response, post-after-discharge enhanced grooming and pleasure reactions, and receptivity to genital stimulation with induced, sustained erection. During conditioned avoidance testing, well-trained cats ordinarily appear quiet and apprehensive. Following hippocampal after-discharge it is striking to see them become preoccupied with grooming and then stretch out in a relaxed attitude on the floor of the shuttle box, fanning their forepaws.

§ In this connection see References 15, 35, and 45.

late gyrus. It has been suggested that the bizarre sexual manifestations[27,55] seen as part of the Klüver-Bucy syndrome may be owing in part to a "release" of some of the structures in question.[35,40]

In conclusion, the following questions come to mind in regard to the pleasure, grooming, and sexual manifestations that have been described: How do they possibly relate to the recent striking observations of Olds and Milner,[44] who found that rats with electrodes implanted in the septum and other limbic structures would repeatedly press a bar to obtain electrical stimulation of the brain? How are they to be considered in the light of the relief of "tension" that some patients experience following psychomotor seizures (personal observations)? And, finally, what possible relevance do they have to the beneficial effects of electroshock treatment, in which, as has been pointed out,[23,29] the hippocampus is especially prone to seizure discharge?

Summary

This paper deals with the behavioral findings following chemical and electrical stimulation of an intermediate segment of the hippocampus in the cat lying between frontal planes A1.5 and A4.5 of Horsley-Clarke coordinates. The preceding communication described a method that allows one to carry out such stimulations in unrestrained animals and at the same time record the electroencephalographic changes. In addition to the technical procedure, the electroencephalographic changes accompanying such stimulations were reported.

For reasons given in Part I, chemical stimulation was usually performed with "cholinergic" agents and involved the application of acetylcholine (and physostigmine), methacholine, and carbachol in crystalline form.

The behavioral manifestations following application of carbachol to the hippocampus correlate with three stages of the electroencephalographic changes: 1. During the stage of development there are few noteworthy findings. 2. When the seizure reaches its height (stage of culmination), pronounced changes occur and are characterized by the animal's lack of spontaneity of movement, pseudocatatonic manifestations, failure to respond appropriately to various manipulations, underreactivity to noxious stimuli of moderate intensity, and sudden vacillation between violent activity and statuesque postures subsequent to intense noxious stimulation. Angry behavior elicited by prolonged noxious stimulation is undirected. Viscerosomatic, postural, and locomotor reflexes are retained. No significant spontaneously occurring autonomic manifestations are evident. 3. During the stage of subsidence the animal manifests enhanced pleasure and grooming reactions and is unusually receptive to genital stimulation. Sustained penile erection may be induced in male cats. If the high-voltage seizure activity associated with Stage 2 fails to develop, these are the only findings.

Except for an apparent enhancement of pleasure and grooming reactions, stimulation with acetylcholine and methacholine was followed by no significant behavioral manifestations that could be correlated with the bioelectrical changes induced by these drugs.

Enhanced pleasure and grooming reactions were observed following 14 of 26 chemical stimulations of the hippocampus. This compared with 2 such positive reactions following 28 stimulations elsewhere. They were not seen when empty needles were placed in the hippocampus. If the results of this exploratory study were subjected to statistical analysis, they would be highly significant.

The foregoing changes in disposition are in marked contrast to the manifestations that occur if the drugs in question escape from the hippocampus into the overlying ventricle. In this event there results a syndrome characterized by contralateral circling, angry behavior, and a number of autonomic manifestations.

The changes that can be demonstrated during hippocampal after-discharges elicited

by electrical stimulation are in most respects similar to those described in regard to Stage 2 of carbachol-induced seizures. For several minutes following after-discharges a majority of animals showed enhanced pleasure and grooming reactions. In the male partial erections were sometimes noted during grooming in the genital region. A comparative study is presented to show that intensive post-after-discharge grooming is also a common finding in the rat. Here, too, one might note the presence of penile erection.

The foregoing experiments are discussed in the light of a number of problems pertaining to experimental psychology and clinical neurology. Continuing investigation is beginning to suggest that a neural system involving parts of the hippocampus, cingulate gyrus, and septum is implicated in the pleasure and grooming reactions and the sexual manifestations that have been described.

Mr. Colin White, associate professor of biometry, and Dr. John Flynn gave help in the statistical aspects of this study.

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Addendum

Since this communication was submitted for publication, an article providing corroborative evidence in regard to the septum has been published by Hess and Meyer (Hess, W. R., and Meyer, A. E.: Triebhafte Fellreinigung der Katze als Symptom diencephaler Reizung, *Helvet. physiol. acta* 14: 397-410, 1956). In an analysis of the extensive material of Hess, the authors found that this was the region (particularly the part near the columns of the fornix) in which electrical stimulation most commonly led to grooming (*Fellreinigung*). Other points were in the cingulate gyrus. The hippocampus was not investigated.

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Posterior Septal, Fornical, and Anterior Thalamic Lesions in the Cat

Vegetative and Behavioral Changes with Anatomical and Physiological Correlations

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Introduction

Investigations of the physiological substrate of behavioral and vegetative mechanisms in the brain have drawn attention to the interdependence of large aggregates of neurons acting upon one another in dynamic equilibrium. Recent interest in the rhinencephalic pathways, as they relate to behavior [9,40,52,53,67,73,82] and autonomic functions,[3, 17,19,22,28,32,39,41,42,49-52,58-62] and in the reticular activating system, with its contribution to the maintenance of consciousness,[4,24,63, 72,83] has led to the present study designed to interrupt these two systems at the junction of the forebrain and the diencephalon. Our attention was originally drawn to this area by the work of Heath and his associates.[38]

Anatomical observations by Rose and Woolsey [78] (1949) and electrophysiological studies by Jasper [47] (1949) suggested that the nucleus reticularis, which forms the oral pole and surrounds most of the thalamus, was well situated to relay widespread cortical responses from the diffuse thalamic projection system. Subsequent observations by Hanbery and Jasper [36] (1953) and Hanbery, Ajmone-Marsan, and Dilworth,[35] (1954) on cortical evoked responses from thalamic stimulation were made before and after acute ablation experiments involving the known specifically projecting thalamic nuclei. These experiments showed that a shorter latency response was recorded from the frontal and motor cortex after stimulation anteriorly in the nucleus ventralis medialis, the nucleus ventralis anterior, and the anterior pole of the nucleus reticularis. From this evidence, it was postulated that the nonspecific multisynaptic pathway passes forward from the centrum medianum and intralaminar nuclei to the oral pole of the thalamus and is relayed through the internal capsule to various cortical areas. The topographical organization showed a relationship of the ventromedial portion of the nucleus ventralis anterior to the frontal cortical regions.

Corticofugal projections were demonstrated by Jasper, Ajmone-Marsan, and Stoll [45] (1952) by recording after-discharge in the diencephalon and midbrain following repetitive stimulation of the frontal pole and cingulate cortex. Local after-discharges, indicating direct projections, were recorded most strongly from the intralaminar nuclei of the thalamus and adjacent portions of the nucleus medialis dorsalis and the nucleus ventralis anterior. Important projections to the subthalamus, hypothalamus, and midbrain occurred also. The precise pathway conducting corticofugal impulses has not been determined. These studies indicate a reciprocal relationship between frontal cortex and the diencephalon.

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A preliminary report of these results was presented at the 112th Annual Meeting of the American Psychiatric Association, Chicago, May 4, 1956.

The anatomical studies of Fox et al.[23] (1944), Le Gros Clark and Meyer[13] (1947), and Brodal[10] (1947) indicate a restricted distribution of primary olfactory afferents in what has been known as the rhinencephalon. On the basis of anatomical and electrographic evidence, Pribram and Kruger[74] (1954) delineated three systems within the rhinencephalic formations: first, a primary olfactory system, based on its direct connections with the olfactory bulb, the olfactory tubercle, the area of the diagonal band, the prepyriform cortex, and the corticomedial nucleus of the amygdaloid complex; second, the basolateral portion of the amygdaloid complex, the septal nuclei, and the subcallosal and frontotemporal juxtallocortex, connected with the first system but not with the olfactory bulb, and, third, the allo- and juxtallocortical systems, made up of the entorhinal, retrosplenial, and cingulate cortex, and the hippocampus (cornu ammonis; Ammon's formation), projecting to the septum and mammillary bodies via the fornix. It is the second system which has been generally implicated in behavioral and autonomic regulation. With these anatomical and electrophysiological observations at hand, electrolytic lesions involving the septum, fornix, and anterior thalamus were made in a series of cats which resulted in a variety of behavioral and vegetative alterations.

Materials and Method

This report is made on the basis of experiments conducted on 85 adult stock cats, weighing from 1.5 to 3.0 kg. Preoperative studies included observations on spontaneous activity, feeding, responses to handling, attention to static and moving objects, grooming, posture, muscle stretch, and pupillary reflexes. Rectal temperatures were recorded. In selected animals, serum sodium and potassium were determined by flame photometry,[87] and whole-blood glucose by the Somogyi method.[84] Serum chloride was determined titrimetrically,[81] as was serum magnesium.[79] Blood urea nitrogen was determined by the urease method.[21]

Operations were performed under sterile conditions with intraperitoneal pentobarbital sodium anesthesia (0.032 gm/kg.). An additional dose of 0.016 gm/kg. was usually necessary to secure adequate anesthesia. With the aid of a stereotaxic instrument, a 22-gauge nicochrome (Nichrome) wire, enamel-coated to 1 mm. of its tip, was introduced into the brain, through a trephine opening in the skull and a slit in the dura. Anodal lesions were produced in the desired locations by the use of a 3 ma. current applied for one minute.

After operation all animals were placed in single cages at room temperature (19 to 28 C). Antibiotics were administered, but no attempts at incubation, forced feeding, or fluid administration were made. Serial behavioral, temperature, and blood studies were then recorded until spontaneous death of the animal or until it was killed, one day to three months postoperatively.

The animals were perfused with saline and 10% formalin through the left ventricle of the heart; the brain was removed and placed in 10% formalin. Serial sections were stained by the Thionine and Weil techniques.

Results

A detailed anatomical analysis of the lesions in the anterior thalamus and septal region of this group of cats was done with the aid of the stereotaxic atlases of Jasper and Ajmone-Marsan,[46] and Jiminez-Castellanos.[48] After a careful review, designed to bring out correlation of results with histological findings, it was found that this analysis could be more satisfactorily accomplished by dividing the area involved in the electrolytic ablations into seven parts (bilateral except where specifically noted).

1. Medial heads of caudate nuclei (frontal plane): A, 16-19 mm. (lateral); R-L, 3-5 mm. (vertical from Horsley-Clarke 0); H, +5 to −2 mm.: caudate nucleus (medial margins of heads), nucleus accumbens

2. Unilateral septum and corpus callosum: A, 16-19 mm.; R-L, 0-2 mm.; H, +7 to −1 mm.: corpus callosum, superior lateral septum, midlateral septum, inferior lateral septum, superior medial septum, midmedial septum, inferior medial septum

3. Bilateral anterior septum and corpus callosum: A, 16-19 mm.; R-L, 0-3 mm.; H, +7 to −1 mm.: corpus callosum, superior lateral septum, midlateral septum, inferior lateral septum, superior medial septum, midmedial septum, inferior medial septum

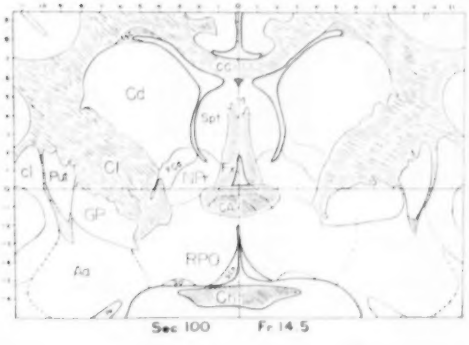
4. Posterior septum and fornix: A, 13.5-16 mm.; R-L, 0-3 mm.; H, +7 to +1 mm.: corpus callosum, superior lateral septum, midlateral septum, inferior lateral septum, superior medial septum, midmedial septum, inferior medial septum, fornix, nucleus prothalamicus, anterior commissure

5. Medial anterior thalamus: A, 10-13 mm.; R-L, 0-3 mm.; H, +8 to −1 mm.: corpus callosum, fornix, stria medullaris, nucleus paraventricularis anterior, nucleus parataenialis, nucleus anterior dorsalis, nucleus reticularis, anterior thalamic radiations, nucleus anterior ventralis, nucleus anterior medialis, nucleus ventralis anterior, nucleus reuniens, lamina medullaris interna, nucleus interanteromedialis, nucleus rhomboidiens, nucleus centralis medialis, nucleus centralis lateralis, tractus mammillothalamicus, nucleus paracentralis, nucleus submedialis

6. Lateral anterior thalamus: A, 10.5-13 mm.; R-L, 4-7 mm.; H, +8 to −1 mm.: stria terminalis, nucleus reticularis, nucleus ventralis anterior, lamina medullaris interna, nucleus ventralis lateralis, nucleus ventralis lateralis dorsalis

7. Medial preoptic region: A, 14-16 mm.; R-L, 0 to 3 mm.; H, −1 to −5 mm.

The anatomical correlations show that lesions in the septum, anterior to the anterior commissure from A 16 to A 19, have produced little or none of the changes seen from more posterior placement. The animals which developed the severe effects under discussion had lesions that destroyed the posterior septum and the anterior parts of the thalamus. There are exceptions, however, to this general finding. Cat 83, for instance, had a very discrete lesion confined to the posterior septum (Fig. 1) and showed profound changes. Cat 70 had almost identical lesions, on the other hand, and showed only minimal signs. Cat 78 had a barely



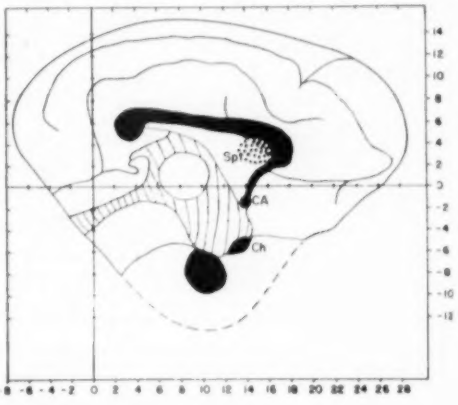
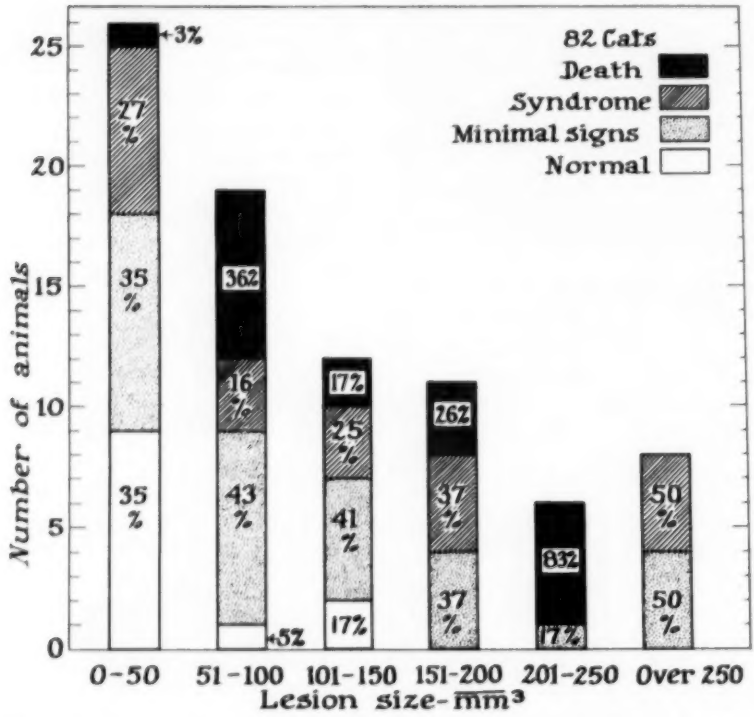


Fig. 1 (Cat 83).—Site of the lesion. Alterations following ablation consisted of coma, hyperglycemia, hypothermia, and spontaneous death.



Effect of lesion size on behavioral and vegetative alterations resulting from ablation. The term "syndrome" refers to coma, hyperglycemia, hypothermia, and spontaneous death.

detectable lesion involving the medial surface of the anterior thalamus on the right side only, and showed a marked temporary hypothermia and hypokinesia. Because the size of lesion per se may well play a role in effects produced by ablations in the nervous system, we have given the estimated volumes of lesion size. In only five animals were they larger than 270 cu. mm., and only one was more than 400 cu. mm. (i. e., 720 cu. mm.). Most of the animals which showed entirely normal behavior following operations had small lesions anteriorly placed in the septum and medial margin of the head of the caudate nucleus. The relationship of lesion size to effect is given in the graph.

Vegetative Changes

There were 20 animals which showed the syndrome of hypothermia accompanied by coma, hyperglycemia, and spontaneous death (Table 1). In addition, 12 animals showed rectal temperatures that reached low levels (under 36 C) for varying lengths of time postoperatively, but did not exhibit the full syndrome (Tables 3 and 4). It is noteworthy that no animal having hypothermia failed to show at least some of the other changes observed in this study.

Of the first group, of 20 cats, 16 had lesions in both the posterior septal and the medial anterior thalamic region. Four of these animals also showed some damage in the medial preoptic area. Four animals had lesions in the posterior septum bilaterally, in one of which the lesion was also associated with medial preoptic injury. One cat with medial anterior thalamic destruction alone, and another with a lateral anterior thalamic, plus a small preoptic, lesion, were included. In the second group, of 12 animals, hyper-

TABLE 1.—*Animals showing coma, hyperglycemia, hypothermia, and death following ablation*

COMA. HYPERGLYCEMIA. HYPOTHERMIA. DEATH.

No.	Survival Days	Med. Hd. of Cd. A16-18	Unil. Spt. A16-19	Bil. Spt. A16-19	Bil. Spt. + Fx. A13.5-A16	Med. Ant. Thal. A10-13	Lat. Ant. Thal. A10.5-A13	Med. R.P.O. A14	Est. Vol. MM³	Temp. C°	Highest Gluc. Postop.	Follow	Hypokinesia	Conscious	
27	9				X	X			144	33.0	175	0	++++	C	D.
30	47				X	X		X	45	31.	419	++++	0	N	D.
33	28				X	X			?	35.5	165	0	++++	C	S. MORIBUND
49	3				X	X			179	25.5	138	0	+++	C	D.
50	4				X	X			63	25.5	215	0	—	C	D. RAGE
51	4				X	X			363	35.5	156	0	+++	S to C	D. BRIEF REACTION TO PAIN
55	12				X	X			140	32.	140	+ to 0	++	S	D. TREADING ATAXIA
75	4				X	X			96	29.5	185	+ to 0	++++	—	D.
77	1				X	X			392	31.	345	—	—	C	D.
81	2				X				24	24.	130	—	—	C	D.
83	2				X				42	25.	225	—	—	C	D.
98	3				X			X	126	33.	160	—	—	S	D.
116	1				X	X			168	35.	150	0	—	C	D. GRASP, JUMP
117	1				X	X			160	32.9	152	—	—	C	D. GRASP, JUMP
128	2					X			13	26.	178	—	—	C	D.
130	1				X	X		X	720	34.	144	—	—	C	D. CONTROL SUGAR 179
131	4				X	X			68	33.	158		++++	C	D. ATAXIA BRIEF RAGE REACTIONS
135	1				X				20	23.	203	—	—	C	D. DIED DURING HT. STRESS
140	5				X	X			13	32.	156	—	++++	C	D.
143	1						X	X LAT.	48	32.	190	—	—	—	D.

TABLE 2.—*Animals showing no alterations following ablation*

BEHAVIOR NORMAL

No.	Survival Days	Med. Hd. of Cd. A16-18	Unil. Spt. A16-19	Bil. Spt. A16-19	Bil. Spt. + Fx. A13.5-A16	Med. Ant. Thal. A10-13	Lat. Ant. Thal. A10.5-A13	Med. R.P.O. A14	Est. Vol. MM³	Temp. C°	Highest Gluc. Postop.	Follow	Hypokinesia	Conscious	
S6	14	X	X						18	38.5	—	0	N	N	Sacrificed
A1	62		X						16	38.	—	0	N	N	S.
A2	40			X					26	39.	—	0	N	N	S.
A3	75			X					30	38.	—	0	N	N	S.
A6	?			X					32	39.5	—	0	N	N	S.
A8	35	X	X						12	—	—	0	N	N	S.
8	81		X						6	39.5	—	0	N	N	S.
26	36			X					112	40.	85	0	N	N	S.
64	9					X			45	38.5	—	0	+ 1day	N	S.
79	11				X				6	38.5	95	0	N	N	S.
102	13				?	?		?	—	39.	—	0	N	N	S.
111	4			X	X		X		84	38.5	—	0	N	N	S.
136	35				X	X			120	39.5	81	0	N	N	S.

TABLE 3.—*Animals showing spontaneous death following ablation*

DEATH No.	Survival Days	Med. Hd. of Cd. A16-18	Unil. Spt. A16-19	Bil. Spt. A16-19	Bil. Spt. + Fx. A13.5-A16	Med. Ant. Thal. A10-13	Lat. Ant. Thal. A10.5-A13	Med. R.P.O. A14	Est. Vol. MM³	Temp. C°	Highest Gluc. Postop.	Follow	Hypokinesia	Conscious	
37	2nd OP. 9				X	X			240	37.5	90	+++	+++	S	JUMP D. POSTURING, RUNNING MOV'TS
48	3				X	X		X	162	24.5	—	—	—	C	D.
52	3					X			158	24.5	—	—	—	C	D.
56	6				X	X			16	37.5	—	0	+++	N	D. ATAXIA
57	3				X				108	39.	—	0	+	S	D. RIGHTING IMPAIRED
100	6				X	X		X	216	41.	148	0	+++	C	D. JUMP, ATAXIA GRASP, RUNNING MOV'TS
102	3rd OP. 2				X	X		X	330	31.5	108	0	++++	C	D. GRASP, JUMP
106	3rd OP. 4				X	X			180	38.5	114	0	++++	C	D. JUMP GRASP, POSTURING
108	7				?	?	?		?	40.	130	0	—	S	D.
110	1				X	X			250	—	—	—	—	—	D.
118	2				X	X	X ANT. HY.		242	31.	—	—	—	C	D. GRASP, POSTURING ATAXIA, RAGE
119	2					X			158	36.	—	—	++	S	D. GRASP
120	2nd OP. 2				X	X			99	40.	60	—	++	S	D.
123	17				X	X			120	37.	57	0	+++	S	D. PILOERECTION OF BACK ATAXIA
127	1				X	X			220	33.	—	—	—	—	D.
139	1					X		X	63	31.5	—	—	—	—	D.
142	½						X		54	34.	—	—	—	—	D.
144	1						X		64	37.5	455	—	—	C	D.
145	1						X		54	34.	—	—	—	—	D. EXTREME GASTRIC DILATATION
147	1						X		52	36.	—	—	—	—	D. RUNNING MOV'TS HEADS OF CAUDATE DESTROYED

glycemia and death were not a constant accompaniment of hypothermia. The lesions were in both the posterior septal and the anterior medial thalamic region in five animals, with the lesion extending to the anterior hypothalamus in one; to the medial anterior thalamic region in three, in one of which it was associated with a medial preoptic lesion; to the posterior septal region bilaterally in one, and to the lateral anterior thalamic region in another.

We did not incubate our animals after operation because we wished to determine the unmodified effect of the lesions. In these circumstances, remarkably low temperatures occurred (Table 1) when the animals were kept at room temperatures of 19-28 C. None of the animals with sustained hypothermia either shivered or panted, nor did they show piloerection. In keeping with the low temperatures were the remarkably low heart and respiration rates. Not uncommonly the heart rate would fall to 30-40 per minute from the normal of 180; respiratory movements fell in frequency to 2-3 per minute.

In those animals which had temperatures below 30 C, the interval between their temperatures and the environmental temperature was very much less than that reported by Clark, Magoun, and Ranson [12] and by Ranson [75] for animals with lesions in the hypothalamus and preoptic region, the latter temperatures ranging in the low and middle 30's, with one temperature reported at 28.5 C, but it is not clear what the environmental temperature was at the time.

To assess the effects of the operative procedure itself, the following studies were made: Thirteen stock animals were given 0.032 gm/kg. of pentobarbital sodium intraperitoneally; eight of these were given an additional 0.016 gm/kg. within an hour.

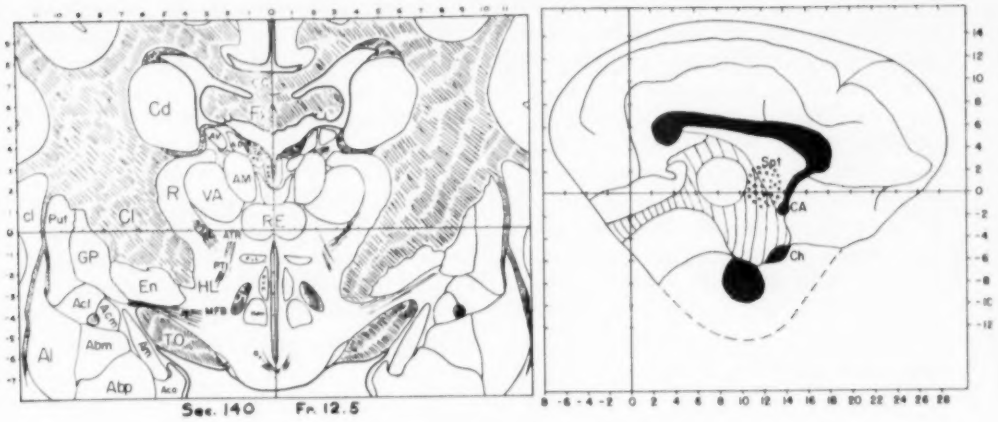


Fig. 2. (Cat 61)—Site of the lesion. Alterations following ablation consisted of hyperglycemia, following, and hypokinesia.

Following onset of anesthesia, a sham operation, consisting of placement in the Horsley-Clarke apparatus, a trephine opening, cutting of the dura, and suturing of the wound, was performed. The temperature was measured at intervals over a 24-hour period. In every instance the temperature was within 1 degree C of the control levels within six hours. The lowest temperature recorded in this series was 34 C. This finding confirms the observation of Ranson[75] (1940), who found a comparable lowering of temperature in cats with hyperthermia of neurogenic origin lasting two to three hours from relatively small doses of pentobarbital sodium. In view of these control observations and the findings of others (Ranson,[75] 1940; McCrum,[70] 1953), temperatures that reached levels below 32 C on the day of operation or those that were below 36 on the first or subsequent postoperative days were considered the result of the neurological lesion, and not of the anesthetic or operative procedure alone.

The low temperatures recorded for the animals showing hypothermia, hyperglycemia, coma, and death (Table 1) all occurred on the first postoperative day, except in three cats, to be discussed below.

Three animals are of interest because of the variation in their temperatures. Cat 33 showed a marked hypokinesia postoperative-

ly, but no fall in temperature until the 24th day. At this time the animal became stuporous, had hyperglycemia, and died. Two cats, Nos. 30 and 55, showed the pattern of an immediate hypothermia, followed by a period of higher temperatures, and then a marked drop in temperature that was concomitant with the death of the animal. Cat 30 had a temperature of 32.5 C on the second postoperative day. This animal had a temperature of 40 C on the fifth postoperative day, which fell to 33.5 C by the 20th postoperative day. The animal lived, however, until the 47th postoperative day, at which time it died, three days following a cold stress. Cat 55 registered a temperature of 32 C on the third and fourth postoperative days. By the 10th postoperative day the temperature had risen to 37 C; by the 12th postoperative day a value of 31.5 C had been reached, and the animal died.

Heat and Cold Stress.—In order to test for latent defects in temperature regulation, as well as to study the effect of warming on hypothermic animals, we exposed 38 cats to both low and high environmental temperatures. The test for reaction to cold was to place the animal in a cold room at 4-5 C for one to two hours. Twenty-two postoperative animals in this series were so tested. Only one animal, No. 75, showed a significant inability to protect against cold (cf. below). Sixteen animals were warmed, some of them several times each. The warming was accomplished by placing the cat in a "hot box," the temperature of which was thermostatically maintained at 45 to 49 C, for periods of one to five hours. Control animals in these circumstances may show a rise in rectal temperature of as much as 2 C. This rise is accompanied by respiratory rates of 250-300 per minute, panting in normal cats becoming prominent when the rectal temperature approximated 41 C. Latent defects were found in Cats 98 and 99. Cat 98 showed a rise in temperature of 3.2 C (37.8-41 C) in 45 minutes at an environmental temperature of 42 C. This elevation was not accompanied by a normal rise in respiratory rate. Instead, the respirations remained between 39 and 52 per minute. Cat 99 showed a rise in temperature of 2.4 C (39.7-42.1 C) in 20 minutes at an environmental temperature of 47-48 C. The respirations rose abruptly from 44 to 138 per minute but did not exceed this rate. The poor respiratory response to such a rise in rectal temperature constitutes a defect in an important mechanism for promoting heat loss. No deficits in these mechanisms were uncovered in the remaining six animals, which had normal temperatures postoperatively.

Warming hypothermic animals showed three interesting phenomena: Panting began at markedly subnormal temperatures (29-35 C); the rate of panting was subnormal (below 200 a minute), and five of eight animals died either during or shortly after the test. The animals tended to become more alert during the warming, and Cat 75 became viciously aggressive at a rectal temperature of 37 C but was docile and stuporous at lower levels. In two of these cats the respirations ceased before the heart beat, suggesting that their death was not due to cardiovascular failure.

Electroencephalograms.—The cortical potentials of hypothermic animals in coma were essentially isoelectric (Fig. 3). As the animals were warmed, however, activity progressively reappeared. This has previously been observed, in animals artificially cooled, by Gaenshirt et al.[27] (1954). Ordinary alerting responses in the EEG could not be tested because of extreme low voltage. Koella and Ballin[56] (1954) found an absence of the arousal response in hypothermic cats below 34-30 C.

Hyperglycemia.—Thirty animals had hyperglycemia. Twenty of the animals showed this abnormality in association with coma, hypothermia, and death (Table 1). In addition, 10 animals had high glucose levels at varying times postoperatively in the absence of one or more of the other signs (Tables 3 and 4). Of the latter group, only one had associated fall of temperature to 32 C, but

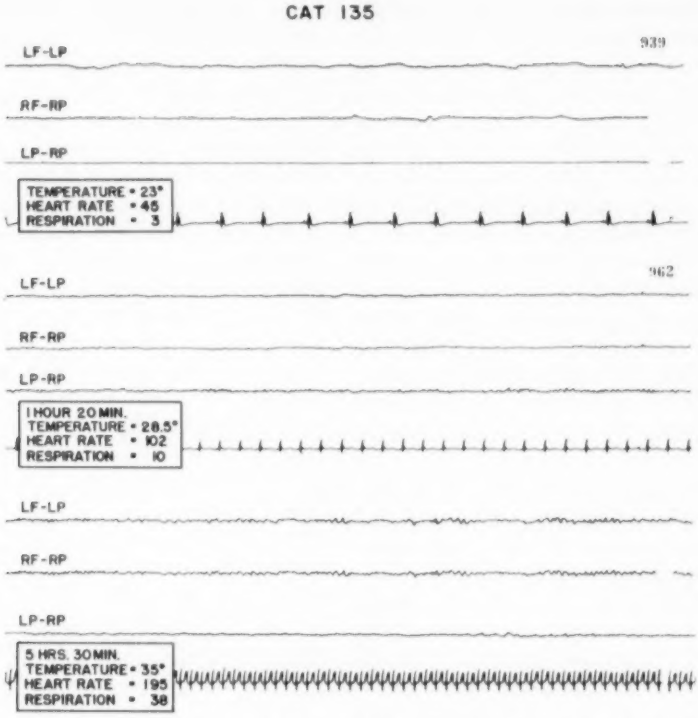


Fig. 3.—Effect of warming on cortical potentials of comatose, hypothermic animals.

behavioral changes or death occurred. In the first group, of 20 cats, 16 had combined posterior septal and medial anterior thalamic lesions, in 5 of which they were also associated with medial preoptic damage. Four animals showed posterior septal damage alone; in one there was isolated bilateral medial anterior thalamic injury, and in another, lateral thalamic and lateral preoptic lesions. In the second group, of 10 animals, 4 had posterior septal and medial anterior thalamic lesions, in 1 of which the lesion was also associated with a medial preoptic injury. In three the damage was confined to the posterior septal region; in two the medial anterior thalamic region was ablated, and in one of these there were lateral anterior thalamic lesions as well.

Control glucose levels taken preoperatively on 50 cats gave a mean value of 90.6 mg/100 ml., with a standard deviation of 22.6 mg. per 100 ml. of whole blood. We have called hyperglycemic those levels of blood glucose which exceeded 113 mg. per 100 ml. This means that only those levels that exceed the mean value by a full standard deviation have been included in this definition.

Because of the well-known hyperglycemic effect of anesthesia and of brain damage,[1] studies were made to evaluate these factors in our animals. Blood glucose levels were determined in five cats given pentobarbital sodium (32 mg/kg.) intraperitoneally, to determine the temperature response. Specimens were drawn immediately after the onset of anesthesia, 4, 6, and 24 hours postoperatively. The sham operation described above was completed within 30 minutes after the onset of anesthesia.

Mild increase in blood glucose levels was observed at four and six hours postoperatively. At the end of 24 hours, however, the levels in every instance were normal. In no

instance did these hyperglycemic values exceed 133 mg/100 ml.

Glucose levels recorded in the Tables as hyperglycemic all occurred at least 24 hours postoperatively. Of the 32 animals showing blood sugars above 113 mg/100 ml., the values for 21 ranged between 150 and 455 mg. per 100 cc. These high levels may take on particular significance in view of the fact that most animals ate not at all, or very poorly, postoperatively and no attempt at substitute feeding was made. High values were recorded in Cat 33 on the 28th postoperative day. The remaining high values were obtained on the first to the seventh postoperative days, usually on the first or second.

Electrolytes.—Determinations of the concentrations of serum sodium, potassium, and chloride were done on 38 cats. These values were grouped according to whether or not they occurred in the control period, during the first to the third postoperative day, or in the period beginning with the fourth postoperative day. While statistically significant elevation, or depression, of the concentration of one, or occasionally two, of the three electrolytes was observed in the postoperative period, these changes occurred infrequently. Furthermore, the occurrence, the magnitude, and the direction of these changes were inconsistent and, in particular, were not correlated with the presence or absence of any of the behavioral or vegetative changes reported in this paper. Blood urea nitrogen determinations were performed on 25 animals, and, again, no significant differences could be detected between control values and those obtained in the postoperative period. Serum magnesium levels were obtained on six animals. On the basis of these few observations, no consistent change in the concentration of this substance could be detected following the operative procedure.

Behavioral Effects

Hypokinesia.—Hypokinesia was observed in 43 cats. Of these, five had bilateral anterior thalamic lesions; the ablation was unilateral in one. This, in general, agrees with the observations of Baird et al.[6] (1951), Schreiner et al.[83] (1953), and Meyer and Hunter[71] (1952), who demonstrated relative immobility and poverty of spontaneous movement to be associated with such lesions. Thirteen cats demonstrated this phenomenon in the presence of bilateral posterior septal injury alone. A combination of these two lesions was found in 21 cats, in which the deficit was most profound, but there was usually considerable or complete clearing of hypokinesia after 7 to 14 days in cats which survived. Two animals in this latter group had associated medial preoptic lesions below the anterior commissure. Of nine cats with lateral anterior thalamic lesions on both sides, only three survived more than 2 days postoperatively, and two of these had marked hypokinesia with recovery over a period of 9 to 14 days. The animals had a marked diminution in spontaneous movement, as noted by Bailey and Davis (1942) after periaqueductal lesions, accompanied by a plasticity of their musculature, such that they would hold awkward postures. They crossed their own legs, leaned off balance, held themselves half-on and half-off a table top, and maintained unnatural postures given them for several minutes. This activity was similar to the "catalepsy," reported by Ingram, Barris, and Ranson[44] (1936) resulting from midbrain injury, and by Meyer and Hunter[71] (1952), who reported similar states from mammillothalamic tract ablation. Characteristically, these animals stood with head and tail down, with the chin barely off the floor. Ambulation was aimless and slow, although in a straight line. It was considerably different from the purposeful, darting, graceful, stop-and-go locomotion of the normal cat, but became a stiff, slow, even pacing. Upon meeting an obstruction, these animals continued their walking motions for a few minutes and then became immobile. The animals did not seem to recognize familiar objects and walked through pans of milk or water, upsetting

them. Their behavior was similar to the "obstinate progression" observed by Bailey and Davis[4,5] (1942) following lesions of the interpeduncular nucleus. The cats gave no sign of recognizing food, other cats, rats, or the observer. When their mouths were brought into direct contact with food or milk, they would sometimes listlessly eat or drink. In their neglect of obstacles, and in the disregard for discrepancies in height, the animals acted as if they were blind. This, however, did not seem to be the case, for the cats would fix their eyes on moving objects when their attention could be obtained.

The corneal and pupillary reflexes remained intact, as did the placing reaction. In the more markedly slowed animals the righting reflexes were impaired commensurate with their deficit. The deep tendon reflexes were present.

Jump Reflex.—A motor phenomenon found in eight cats was the "jump reflex," which had been described previously by Guzman and del Pozo[34] (1953) after decerebration to the hypothalamic level. This reflex is elicited when the pads of the hindfeet are touched to the floor and is more easily demonstrated if the neck is forcibly extended, then flexed. Following this, there occurs a powerful extensor thrust of the hindlimbs, making the animal jump 6 to 18 in. into the air, accompanied by random, pawing movements of the forelimbs. It is characteristic of animals in which this reflex is elicitable that there is marked downward extension of the hindlimbs and of the forelimbs when they are lifted by the scruff of the neck.

Guzman and del Pozo's animals, in contrast to ours, showed rage as well. All of the animals which had the "jump reflex," and none which did not, had a tendency to "grasp." Grasping consisted of a strong flexion at the distal joint of the forelimbs when pressure was exerted proximal to the foot pads. These animals would hang, supported only by this "wrist action," for periods up to a minute at a time. The animals' claws remained sheathed. This phenomenon was described by Ingram et al.[44] (1936) in their description of "catalepsy" resulting from the lesions made in the reticular formation rostral to the red nucleus. The most striking aspect of the jump-and-grasp activity of these animals was the great vigor with which these responses were made by animals which otherwise appeared weak, and, indeed, were moribund.

State of Consciousness and Emotional Expression in Hypokinetic Animals: The state of consciousness of the animals described here was characterized by "withdrawal" in the sense that they paid little or no attention to cats, rats, or the observer. They were remarkably unresponsive to pain. A moderate pinch, for instance, would elicit a slight response. A severe one might provoke vocalizing, with feeble and transient attempts to escape or attack the source of the stimulus. No rage reaction or coordinated attack could be elicited with rough handling. The animals were indifferent to food and drink. They showed no sexual interest. There was a marked lack of grooming. The inquisitiveness of the normal cat was entirely absent. The apparent failure to recognize familiar objects, and perhaps the posturing, may indicate an altered state of consciousness. The placidity of behavior seems identical with that reported by Bard and Mountcastle in cats in which all neocortex was removed, sparing the temporal lobes and the medial transitional cortex. One cat which was severely hypokinetic and hypothermic showed marked bursts of rage when it was warmed (Cat 75). Three cats (50, 118, and 131) showed brief rage reactions to minimal stimulation. One of these animals (118) had, in addition to the posterior septal and anterior medial thalamic lesions present in the other two, lateral anterior thalamic and hypothalamic damage.

Compulsive Following.—Another prominent effect attributed to decortication (Dusser de Barenne and Magnus,[18] 1920; Bard and Rioch,[8] 1937), frontal and caudate in-

jury (Mettler,[69] 1942), frontal lobe ablation (Magoun and Ranson,[67] 1938; Wheatley,[90] 1944), and a large diencephalic lesion (Ingram,[43] 1952) was a marked tendency to follow moving objects in a compulsive fashion. We have been conservative in estimating the amount of following shown by our animals. It was observed to occur in 14 cats and was estimated by us to be 3+ or 4+, on a scale of 1 to 4. The lesions included both posterior septal and anterior medial thalamic regions in five; the posterior septum, in five, in one of which it was unilateral; the anterior septum unilaterally in one, the medial anterior thalamus in one, and the lateral anterior thalamus in another, and for the last anatomical data were inadequate. These animals were alert, hyperactive, and affectionate. They sought contact by rubbing their arched backs against the observer's legs and, less frequently, against inanimate objects. As early as the first postoperative day they showed pronounced interest in following, to the extent that they could be easily induced to follow a visually perceived finger or pencil in a circle having a radius as small as 6 in. They would follow a walking man as though tied to him, but would sometimes break this connection to follow someone going in the opposite direction. After walking 300 to 400 ft., some cats tired markedly—would sit for a few minutes and then, apparently restored, would resume "compulsive" following. These animals constantly sought rubbing and petting—arching their backs and approaching the "presenting" position of the erotically aroused cat, but never fully reaching it. There was associated, persistent piloerection of the base of the tail in two animals and over the back in two, unilaterally in one of them. This group at first seemed to sleep little, and seldom to lie down. The cats had little interest in food—none at first, then gradually more, until, at the end of two to three weeks, they ate quite normally. A constant flexing of the toes of the forepaws, which were frequently lifted, was observed in four animals. This "treading" phenomenon has been noticed by Bard and Rioch[8] (1937) after decortication and injury to deeper structures, after bilateral frontal lobe ablation by Magoun and Ranson[67] (1938) and after combined anterior and mediodorsal thalamic lesions by Schreiner et al.[83] (1953). This action was remarkably similar to the forepaw action of nursing kittens. At times this "forepaw treading" took on marked erotic coloring, and on one occasion a cat carried this action out extremely vigorously and intensely on the body of a hypokinetic cat. This lasted for a full 15 minutes without interruption. Through an error, this cat was subjected to a second operation on the 31st postoperative day and had multiple (48) small lesions placed throughout the A−5 plane. These extensive lesions at a completely different location ultimately changed the cat's behavior not at all. Cortical blindness, however, was produced for a period of one week, after which the activity was resumed, illustrating the dependence of the "following" response on visual stimuli.

Mortality

Of the total number of 85 stock cats in which lesions were made, 40 died prior to being killed (Tables 1, 3, and 4). They may be divided into two groups. The first group, of 25 animals, died within 72 hours after operation. The second group, of 15 cats, survived from 4 to 47 days, only 4 of these animals dying after the 9th postoperative day. Animals in both groups had bilateral lesions. Twenty-five animals had posterior septal and medial anterior thalamic lesions, five of these also showing some encroachment on the medial preoptic area. Anterior lateral thalamic injury was present in six, two of which also had medial preoptic or anterior hypothalamic damage. Five had posterior septal lesions, and in the remaining four deaths were associated with medial anterior thalamic damage alone. Prolonged hypothermia, below 32 C, occurred in 14 of these animals. Lowering of body temperature alone seems unlikely as an isolated

TABLE 4.—*Animals showing behavioral and vegetative signs without death*

No.	Survival Days	Med. Hd. of Cd. A16-18	Unil. Spt. A16-19	Bil. Spt. A16-19	Bil. Spt. + Fx. A13.5-A16	Med. Ant. Thal. A10-13	Lat. Ant. Thal. A10.5-A13	Med. R.P.O. A14	Est. Vol. MM³	Temp. C°	Highest Gluc. Postop.	Follow	Hypokinesia	Conscious	SIGNS WITHOUT DEATH
A7	36			X					28	—	—	0	++	N	Sacrificed
57	9	X				X			392	38.	—	0	+++	N	S
25	76			X	X				120	39.5	—	0	+→0	N	S
28	43				X				140	39.	200 — 66	+++	+++	N	S EXHAUSTIBLE
29	27				X	X			173	32.	135	+→0	+→0	N	S FOLLOWING APPEARED 12th d. HYPOKINESIA DISAPP'D 12th d.
31	26				X				270	39.5	50	0	+→0	N	S
34	29				X				165	38.5	65	+++	+→0	N	PILOERECTION OF TAIL S EXHAUSTIBLE
37	1st OP 33				X	X			240	39.	—	+→0	+→0	N	S
38	27				X				45	38.5	70	+→+	+→++	N	S PILOERECTION OF TAIL
39	2nd OP 20				X				120	40.5	—	0	+→0	N	S RIGHTING MARKEDLY IMPAIRED
59	16				X				72	38.5	—	+→0	+→0	N	S SIGNS CLEARED 12th day
61	16					X			140	36.5	121	+→0	+→0	N	S CLEARED 10th–11th day
62	15				X	X			47	38.5	—	+→0	0→+	N	S SEPTUM MINIMALLY DAMAGED FOLLOWED TILL 5th d. only
63	10					X			72	37.	—	+→+	+→0	N	S HYPOKINESIA CLEARED ON 8th day
66	10				X	X			84	38.5	—	0	+→+	N	S
69	8				X				50	38.5	—	+→+	0	N	S PILOERECTION OF TAIL FOLLOWING STOPPED 7th d.
70	12				X				44	38.5	—	+→0	+→0	N	S PILOERECTION OF PROXIMAL TAIL
72	7				X	X			102	37.5	—	0	+→+	N	S
76	48				X	X			192	38.5	138	+→++	0	N	S SEVERE PERSISTENT ATAXIA
78	3					UNIL. X			4	26	95	+	+→++	N	S PILOERECTION DIED AFTER ½DOSE OF NEMB.
84	10		X						5	39.5	55	+→0	0	N	S
89	8				X				36	39.	115	+→0	+→0	N	S
91	8				X	X			?	39.5	44	0	+++	N	S
99	76				X	X			264	40.3	—	++++	0	N	FOREPAW TREADING S HYPERREFLEXIC EXHAUSTIBLE
109	90					X			43	39.	127	+→0	0	N	S
115	22				X	X			175	38.	41	0	+→0	C	JUMP S GRASP
120	15				X				99	41.5 34	—	0	++++	S	S
137	16				X	X			70	34.	90	+++	+ 2nd d.	N	FOREPAW TREADING S PACING
138	34	MASSIVE DESTRUCTION CINGULATE 2nd FORNIX			SEPT. X				252	39.	69	+→0	+→0	N	S CLEARED BY 6th day
141									84	40.	—	+→0	—	N	S
146	17						X		60	38.	78	0	+→+	N	S PILOERECTION OF TAIL
149	72						X		100	38.5	94	+→++	+→0	S→N	S

cause of this high incidence of mortality. Electrolyte disturbance and blood urea nitrogen were studied and were not found to be consistently altered. The initial lack of ingestion of fluid and food was not a significant factor, since several cats not operated on were isolated without food or water for a period of more than seven days without causing death. The animals did not have diarrhea, nor were they involved by any infectious disease as far as was clinically discernible. The lungs and other organs were examined and appeared grossly normal at autopsy. No histologic sections other than those of the neural tissues were studied.

Comment

We have been only partially successful in localizing the lesion that gives rise to the behavioral and vegetative changes reported here. In consecutive animals, groups which showed behavioral and vegetative changes were interspersed with groups which showed none, despite virtually identical lesions. Actual variation of the location and size of the area destroyed does not seem to be a satisfactory explanation. If it were, the critical areas responsible would, of necessity, be exceedingly small. It would seem more plausible that a multiplicity of conditions is

requisite for the occurrence of the changes observed in these animals. Such multiple factors may include potentiation of anesthetic effect, circulatory changes, edema, and submicroscopic neuronal damage. It is likely that the location and extent of the anatomical lesion is but one of these variables. It is clear, however, that placement of the lesions in the area of the posterior septum, fornix, and anterior thalamus was a most critical determinant. Anterior septal ablations were not associated with a deficit. Anatomical and physiological evidence indicates that the posterior septum is in the pathway from the amygdaloid complex and hippocampus to the hypothalamus. Recent electrophysiological observations in the cat reported by Gloor[30,31] (1955) following stimulation of the basolateral amygdaloid complex have shown a primary projection area, on the basis of short latency responses, to the base of the septum, the nucleus accumbens, the preoptic area, and the anterior hypothalamus, as well as to the frontotemporal cortex (orbital gyri, insula, and temporal pole). Longer latency responses show evidence of projection to the corticomedial subdivision of the amygdala, the hippocampus, the remainder of the hypothalamus, the subthalamus, parts of the diffuse thalamic projection system, and the tegmentum of the upper brain stem. Anterior thalamic lesions interfere with the activating system at the point of its emergence from the anterior pole of the thalamic reticular nucleus.[35,36] The electrophysiological studies of Feindel and Gloor[29] (1954) show that stimulation of either the amygdala or the brain stem reticular formation diffusely alters cortical activity in an almost identical manner. These authors postulate (1) that the amygdala may discharge back into the brain stem reticular formation, which, in turn, activates the cortex; (2) that the amygdala may act as a relay through which the effect of stimulation of the brain stem reticular formation is mediated to the cortex, and (3) that both the amygdaloid and the reticular effects may be independent but that the responses are dependent on mechanisms activated at a cortical level. Both systems are known, however, to exert diffuse regulatory effects on other cerebral regions and have been found by Green and Arduini[33] (1954) to have an inverse relationship in that desynchronization associated with arousal, as seen in the cortex, induced by a variety of external stimuli or by direct excitation of the reticular activating system in the brain stem, is associated with the concomitant appearance of an undulating series of large slow waves in the hippocampal record. This hippocampal response can be prevented by septal lesions and by section of the dorsal fornix in the rabbit and cat.

Hypothermia associated with lesions superior to the preoptic region and hypothalamus occurred in 32 of our animals. Heath[38] (1954) reported depression of body temperature following the placement of somewhat larger lesions in this general area. Heath's lesions extended farther anteriorly and below the level of the anterior commissure.

The cats with marked hypothermia in our series were poikilothermic, as evidenced by their response to changes in environmental temperature, including heat and cold stress. The absence of shivering and piloerection in the hypothermic cats indicates a loss of heat-producing and heat-conserving mechanisms. The occurrence of panting during warming, when the temperature was as low as 28 C, is an unusual finding, showing resistance to warming suggestive of an altered thermostatic setting. The constant association of other changes in all animals exhibiting hypothermia demonstrates that it is imperative to study temperature regulation as an integral part of over-all mechanisms that involve state of consciousness, emotional expression, muscular activity, and other vegetative changes. The origination of electrical activity in the limbic system upon arousal of the golden hamster from hibernation, as observed by Chatfield and Lyman[11] (1954), supports the thesis of

widespread integration in the control of body temperature.

Transient hypothermia followed by hyperthermia, reaching a peak (a rise of 1.6 degrees (C) or more) in 6 to 8 hours, with return to normal within 24 hours after brief electrical stimulation of the lateral amygdaloid nucleus on one side in the cat, was reported by Koikegami, Kushiro, and Kimoto[58] (1952). They found that section of the fornix or the stria terminalis did not obliterate this response but that unilateral destruction of the hypothalamus on the side stimulated did prevent the hyperthermia. Gloor[30,31] demonstrated projections from the basolateral amygdaloid complex, interruption of which in our ablations in this area may have accounted for the observed hypothermia.

We were unable to determine the precise cause of the high incidence of early and late postoperative mortality. The potentiating effect of hypothermia on barbiturate anesthesia,[25,77] with the major site of action of both on the reticular activating system,[56] may account for some of the early deaths. Death following large bilateral hypothalamic lesions has been noted by Clark, Magoun, and Ranson[12] (1939) and by Massopust et al.[68] (1954), which they attributed to starvation, diarrhea, or increased susceptibility to infection. None of these conditions was an apparent factor in our animals, and only the sum total of the vegetative defects here reported, plus others which were not observed, can be invoked to explain this finding.

It is noteworthy that each of the phenomena which we have observed has been described by others in the cat as a result of lesions in which usually considerably larger amounts of tissue have been destroyed in this and other regions—for example, hypokinesia, from lesions of the periaqueductal gray matter (Bailey and Davis,[4,5] 1942), and obstinate progression, associated with frontal lobe and caudate nucleus ablation (Mettler,[69] 1942) and after destruction of the interpeduncular nucleus (Bailey and Davis,[4,5] 1942). Compulsive following has been identified with decerebration (Dusser de Barenne and Magnus,[18] 1920; Bard and Rioch,[8] and Wheatley,[90] 1944), frontal lobe ablation (Magoun and Ranson,[67] 1938), or a large diencephalic lesion (Ingram,[43] 1952); "catalepsy" with muscular plasticity and sustained grasping has resulted from injury to the mammillary-posterior hypothalamic region (Ingram, Barris, and Ranson,[44] 1936); the "jump reflex," from decerebration to the hypothalamic level (Guzman and del Pozo,[34] 1953); placidity of affect, from lesions of the mammillothalamic tract (Meyer and Hunter,[71] 1952), and exaggerated pleasure reactions, from midline transitional cortex removals (Bard and Mountcastle,[7] 1948) and after anterior thalamic ablations (Schreiner et al.[83] 1953). The over-interest in, and the increased motor activity in response to, visual stimuli, as well as the docility reported here, were similar to the behavioral changes reported following injury of the pyriform cortex, amygdaloid nuclei, and adjacent structures by Schreiner and Kling[82] (1953). The exaggerated oral behavior and hypersexuality observed by them were not apparent in our animals.

Rage reactions, savageness, and irritability were conspicuously absent except for three animals in this series, one of which had an additional hypothalamic lesion. Such reactions have been observed in cats after orbitofrontal ablations (Kennard,[54] 1945), injury of the cortex immediately rostral to the optic chiasma (Fulton and Ingraham,[26] 1929), destruction of the ventromedial hypothalamic nuclei (Wheatley,[90] 1944), mediodorsal thalamic nuclear lesions (Schreiner et al.,[83] 1953), and bilateral cingulate and hippocampal lesions in combination with neocortical ablations (Bard and Mountcastle,[7] 1948). We were unable to corroborate the findings of Spiegel, Miller, and Oppenheimer[85] (1940), who reported rage reactions occurring early in the postoperative period in four cats with lesions of the septum and fornix. Wheatley[90] (1944) did not

observe rage reactions following lesions in this area.

Anatomical studies in monkeys utilizing the Glees silver technique (Clark and Meyer,[14] 1950) indicate a massive projection from the frontal pole via the medial forebrain bundle to the ventromedial hypothalamic nuclei. A pathway from frontal cortex to hypothalamus was demonstrated by Ward and McCulloch[89] (1947) by means of strychnine, although specific projection to the ventromedial hypothalamic nuclei was not among their findings. Strychnine neuronography also revealed connections between the orbital gyri and the medial forebrain bundle, as well as the lateral preoptic area just posterior to the anterior commissure, in a study by Sachs, Brendler, and Fulton[79] (1949). These physiological observations were also made in the monkey. Ranson and Magoun[76] (1933) elicited motions of spitting by electrical stimulation of the subfornical component of the medial forebrain bundle in the cat, with probably other than physiological parameters of excitation, but not from the preoptic region or medial anterior hypothalamus. The anatomical analysis of our sections shows sparing of the medial forebrain bundle, at least unilaterally, in almost all instances. This finding suggests that the frontal neocortex in the cat may mediate an inhibitory effect on rage reactions via the medial forebrain bundle to the hypothalamus.

Impairment of consciousness has been correlated with lesions of the reticular activating system (Lindsley et al.,[63] 1950) and thalamic intralaminar ablations (Schreiner et al.,[83] 1953). Hypothermia has been principally associated with destruction in the hypothalamus[68,70] and derangement in glucose metabolism from lesions in a variety of anatomical sites, most strikingly after pontine transections.[1] Control of piloerection has been shown to have widespread representation in the cortex and brain stem.[88] Hypernatremia and hyperchloremia have been associated with injury to the basal forebrain-diencephalic junction observed in the rat (Stevenson et al.[86] 1950), cat (Lewy and Gassman,[64] 1935), and man.[2,15] We were unable to document any consistent electrolyte abnormality in this series of animals, and we would presume the absence of any postulated osmoreceptors (Verney,[91] 1947) in the areas studied.

The occurrence of such a multiplicity of alterations from relatively small lesions in so restricted an anatomical site suggests that the posterior septum, fornix, and anterior thalamic region constitute a pathway through which funnel anatomical elements which exert profound influence on diverse vegetative and behavioral functions.

Our results may be explained on the basis of interruption of the rhinencephalic pathways and the diffuse thalamic projections or the reticular activating system by posterior septal, fornical, and anterior thalamic lesions.

Summary

A variety of behavioral and vegetative changes were observed in 85 stock cats for periods ranging from 1 to 90 days following relatively small, bilateral, stereotaxically placed lesions in the septum, fornix, and anterior thalamus, which were histologically verified and analyzed. These alterations included impaired consciousness, hypokinesia, muscular plasticity, sustained grasping, the "jump" reflex, piloerection, marked hypothermia, and relatively persistent hyperglycemia, as well as a high incidence of early and late postoperative deaths. Rage reactions were conspicuously not in evidence. These results could not be anatomically correlated with discrete nuclear masses or their specific projections. The highest incidence of abnormality was associated with a combination of posterior septal, fornical, and anterior thalamic destruction. Such lesions are so situated as to interrupt major rhinencephalic-hypothalamic and mesencephalic reticulothalamocortical projections, which are thought to account for the observed alterations. Serum sodium, potas-

sium, and magnesium and blood urea nitrogen determinations, before and after the placement of lesions, showed no consistent changes.

Miss Kate Gruen assisted in preparation of the histologic sections. Portions of Figures 1 and 2 are from "A Stereotaxic Atlas of the Diencephalon of the Cat," by H. H. Jasper and C. Ajmone-Marsan,[66] and are reproduced with premission of the publisher, The National Research Council of Canada.

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CORRECTION

In the article "Cranial Nerve Syndromes Associated with Nasopharyngeal Malignancy," by Drs. Helena E. Riggs, Charles Rupp, Homer Ray, and Joseph C. Yaskin, in the May, 1957, issue of the Archives (pp. 473-482), the third line of the second column on page 480 should precede the last line of the first column. The final sentence of the first column should read: "Intracranial extension was absent in Case 4, but actual destruction of cranial nerve foramina in the posterior fossa could be demonstrated."

News and Comment

ANNOUNCEMENTS

Residency in Neurology.—A three-year approved residency in Neurology has been inaugurated at the Bronx Municipal Hospital Center and the Albert Einstein College of Medicine, Yeshiva University. The residency program is supported by a training grant from the National Institute of Neurological Diseases and Blindness. The Division of Neurology of the Department of Medicine at present consists in three full-time physicians. Two separate wards of the general medical service have been assigned to Neurology. The two wards have a total of 60 beds. There are clinical research laboratories, in direct conjunction with the wards. In addition to the clinical training in neurology, an extensive fellowship program in the sciences related to the nervous system is offered to the residents in neurology on an interdisciplinary basis.

Sherrington Centenary.—This is the centenary year of the birth of Sir Charles Scott Sherrington, O.M., a founder and main architect of the physiology of the nervous system. The Royal Society of Medicine, wishing to pay tribute to his life and work, proposes to raise a fund toward a Sherrington Lecture, for the furtherance of knowledge on the nervous system, to be delivered from time to time in the Society's rooms in London.

It is felt that many will wish to contribute: both those who were his friends, pupils and colleagues, and those, more numerous, who, as patients, doctors and scientists, have benefited indirectly from his work.

We wish to take this opportunity to commend the endeavor of the Royal Society of Medicine to establish this memorial to a great pioneer in scientific medicine.

Donations should be made payable to the Secretary, The Royal Society of Medicine, 1 Wimpole Street, London W.1, and checks crosses "Sherrington Memorial."

GENERAL NEWS

Study of Sarcoidosis.—Five Veterans' Administration Hospitals, located in Atlanta, Ga.; Dallas, Texas; Madison, Wis.; New York City, and Washington, D. C., have begun a study of the cause and nature of sarcoidosis.

Books

BOOK REVIEWS

Tumores intracraneales. Edited by S. Obrador Alcade and J. Sanz Ibañez. Pp. 456. Editorial Paz Montalvo, Antonio Maura, 13. Madrid, 1955.

This monograph of the National Institute of Oncology of Madrid consists of a collection of reports by seventeen authorities (fourteen Spanish and three others) of a course given at Santader, Spain, in August, 1955. It is divided into chapters on history, pathology, diagnosis, and treatment. On the whole, the presentations are excellent reviews, and will be valuable for the student and house officer but too elementary for the practiced neurosurgeon.

The most rewarding section is that devoted to pathology, in which Zülch presents his experience with more than 4000 cerebral tumors, discussing genesis and malignancy from the point of view of classification, as well as of clinical behavior. Other papers on pathology by Sanz Ibañez, Calvo, Oliveras, Rocca, and Morales are excellent and beautifully illustrated. In the discussion following the presentation of these papers, Obrador Alcade emphasized the importance of harmonizing the various classifications to reach a unification which would express clearly the histological, genetic, and clinical evolution with tumor localization. The resulting classification grouped cerebral tumors as mature (polar glioma, oligodendroglioma, astrocytoma, ependymoma, pinealoma, gangliocytoma, papilloma of the plexus, and neurinoma) and immature (medulloblastoma, glioblastoma multiforme, neuroblastoma, and carcinoma of the plexus).

There is no bibliography.

A Follow-Up Study of War Neuroses. By Norman Q. Brill and Gilbert W. Beebe. Price, $1.50. Pp. 393. Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

This publication summarizes a large-scale systematic study of neuroses in World War II, offering voluminous evidence for the authors' conclusions and recommendations.

The data indicate that, although predisposition as well as military stress contribute to psychiatric breakdown, it is not possible to identify at preinduction examination those men who will later become psychiatric casualties. Had all psychiatrically predisposed men been rejected at the induction station, the Army would have lost the service of 1,000,000 men who served without psychiatric hospitalization.

As seen five years after discharge, the net effect of psychiatric breakdown in military service is not as great as might have been expected. Little change was found in men who were normal before induction. In those who were not, combat resulted in greater disability than did other forms of military stress.

Manpower reserves are discussed in relation to military necessities. On the basis of their analyses of all available data, the authors recommend for general immobilization that psychiatric screening be confined merely to the elimination of the obviously unfit, that decision about doubtful cases be deferred until completion of a test of service, and that all men otherwise acceptable be inducted. The lack of adequate criteria for evaluating military performance is noted.

BOOKS RECEIVED

The books on the following list have been received and are acknowledged by the Editor of the Section on Neurology of the ARCHIVES.

Paper Electrophoresis (Ciba Foundation Symposium). By G. E. W. Wolstenholme and Elaine C. P. Millar. Price $6.75. Little, Brown & Company, 34 Beacon St., Boston, 1956.

Beyond Laughter. By Martin Grotjahn, M.D. Price, $6.00. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1957.

Libro de communicaciones neurocirugia (journal). March, 1956.

Les Craniopharyngiomes en oto-neuro-ophtalmologie, Reunion interregionale, March 27, 1955.

Hypothalamus und Thalamus—experimental—Dokumente. By W. R. von Hess. Price, $8.60. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N (American Zone), 1956.

Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin Diagnostik, Physik, Biologie, Therapie (journal). Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N (American Zone), January, 1957.

Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin Diagnostik, Physik, Biologie, Therapie (journal). Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N (American Zone), December, 1956.

Revue française d'études cliniques et biologiques. Vol. 1. March, 1956.

Studies on the Morphogenesis of the Brain in Struthio Camelus L.: VI. Morphogenesis of the Vertebrate Brain. By Knud H. Krabbe. Ejnar Munksgaards Forlag, Norregade, 6, Copenhagen, K, 1956.

My Minds and I: Spiritual Psychology, Mental and Physical Well Being. By E. V. "Ted" Crane. Price, $4.00. Christopher Publishing House, 1140 Columbus Ave., Boston, 1957.

Understanding Human Behavior. By James L. McCartney. Price, $3.50. Vantage Press, Inc., 120 W. 31st St., New York 1, 1956.

Journal of the Hillside Hospital. Israel Strauss Commemorative Volume. The Society of the Hillside Hospital. International Universities Press, Inc., 227 W. 13th St., New York 11, 1956.

Practice of Psychiatry in General Hospitals. A. E. Bennett and others. Price, $4.00. University of California Press, Berkeley 4, Calif., 1956.

The Sexual Criminal: A Psychoanalytical Study. By J. Paul De River, M.D. Price, $6.50. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1956.

The Psychology of Sex Offenders. By Albert Ellis, Ph.D., and Ralph Brancale, M.D. Charles C Thomas, Publisher, 301-302 E. Lawrence Ave., Springfield, Ill., 1956.

Principles and Technics of Rehabilitation Nursing. By F. L. Terry and others. Price, $5.50. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis, 1957.

Auge und Zwischenhirn (journal). Ferdinand Enke, Hasenbergsteige 3, (14a) Stuttgart, W, 1955.

Krampfbereitschaft. By Gerhard Koch. Edizioni dell'Istituto Gregorio Mendel, 1955.

Book of Health (Pocket Book edition). Edited by W. W. Bauer, M.D. Price, 35c. Dell Publishing Company, 261 Fifth Ave., New York 16, 1956.

Neurotic Interaction in Marriage. Edited by Victor W. Eisenstein, M.D. Price, $5.50. Basic Books, Inc., 59 Fourth Ave., New York 3, 1956.

Mental Health Planning for Social Action. By George S. Stevenson, M.D. Price, $6.50. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1956.

Educating Spastic Children. By E. Eleanor Schonell. Price, $6.00. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

Women of Forty. By M. E. Landau, M.D. Price, $2.50. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

How to Live 365 Days a Year. By John A. Schindler, M.D. Price, $4.95. Prentice-Hall, Inc., 70 Fifth Ave., New York 11, 1956.

L'Hospitalisation des poliomyélitiques à la phase aigue. Masson & Cie, 120 boulevard Saint-Germain, Paris 6e, 1954.

Jubile du docteur. By J. Andre Thomas Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1956.

Selected Papers of Sir Gordon Holmes. Edited by J. M. R. Walshe. Price, 20 s. Pp. 276. Macmillan & Co., Ltd., 10 St. Martin's St., London, W. C. 2, 1956.

Boston University Medical Science and Society (University Lecture). Chester Scott Keefer, M.D., 1956.

Behringwerkmitteilungen. Begründet von E. von Behring, 1956.

Viruserkrankungen des Menschen. By Dr. Med. W. D. Gerner. Price, $7.15. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N (American Zone), 1954.

La Psychologie appliquée. By Fernand Nathan. 1956.

Aging in Transient Tissues. Editors of the Ciba Foundation. Price, $6.75. Little, Brown & Company, 34 Beacon St., Boston 6, 1956.

The Great Physiodynamic Therapies in Psychiatry. Edited by Ibanez, Sackler, et al. Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 49 E. 33d St., New York 16, 1956.

How to Enjoy Good Health. Edited by Cyril Solomon and Brooks Roberts. Price, $3.95. Random House, Inc., 457 Madison Ave., New York 22, 1956.

Alcoholism as a Medical Problem. Edited by H. D. Kruse, M.D. Price, $3.00. Paul B. Hoeber, Inc., (Medical Book Department of Harper & Brothers), 1956.

The Primary Psychiatric Syndromes. By Dwight L. Moody. Price, $7.50. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1956.

Steegmann Examination of the Nervous System. By A. Theodore Steegman, M.D. Price, $3.75. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1956.

Bone Structure and Metabolism. Editors of the Ciba Foundation. Price, $8.00. Little, Brown & Company, 34 Beacon St., Boston 6, 1956.

Sleep: The Way to Sound and Healthful Slumber. By Marie Stopes, M.D. Price, $3.00. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

Emotional Problems and What You Can Do About Them. By William B. Terhune, M.D. Price, $3.00. William Morrow & Co., Inc., 425 Fourth Ave., New York 16, 1955.

Medical Progress. Morris Fishbein, M.D., Editor. Price, $5.50. The Blakiston Company (Division of) McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1956.

The Happy Life of a Doctor. By Roger I. Lee, M.D. Price, $4.00. Little, Brown & Company, 34 Beacon St., Boston 6, 1956.

SECTION ON
PSYCHIATRY

Perception Experiments in a Study of Ambivalence

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This investigation is concerned with the perception aspects of a larger study on the problem of ambivalence. The over-all goal in the total project is to find specific etiological factors which can be correlated with success or failure in the resolution of ambivalence. These etiological factors deal with the character of the object relations in early life, the opportunities for object relations in general, and, more specifically, the opportunities for warm object relations. Against these etiological factors a set of measurements of the resolution of ambivalence is being worked out. Two of these measurements are presented in this study. One measurement is a structured interview in which we classify our subject material according to degrees of organization or failure in the handling of impulses. The other measurement is a tachistoscopic perceptual test, a measurement of the accuracy of perception and also measurement of the range and breadth of subsequent visual imagery. In working out certain measurements which reflect the state of the ambivalence, we are concerned with the internal and theoretical consistency of our various measurements. It is the correlation of these two mentioned measurements which will be discussed in this paper, i. e., the classification via interview and the perception-imagery measurements.

Some theoretical discussion of ambivalence is necessary to define our concepts and procedures. Although psychoanalytic theorists are by no means in complete agreement about ambivalence, certain aspects of it in general may be stated. In the developing infant and child the feelings of love and hate are not integrated. When a person or situation elicits love, the child will feel that; and if the situation or that same person elicits hatred, the child will feel that. However, with the development of the ego structure and the growing ability to form relationships to specific persons, the child will become aware of conflicting feelings toward one person. As he matures, there occurs a fusion of these separate feelings of hatred and love into a more mature attitude, compounded of the two. This is known as the fusion of the ambivalence and occurs unconsciously, although there are many conscious derivatives. It is the fusion of the ambivalence which characterizes normal object relations. In this state the individual will not feel pure, unalloyed hatred. That would be sheer infantile aggression. In the mature person the hatred is tempered by love. In various mental disorders there are

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From Hillside Hospital, Glen Oaks, N. Y.

Somewhat enlarged from a paper read before a joint meeting of the New York Academy of Medicine, Section of Neurology and Psychiatry, and the New York Neurological Society in New York, Jan. 8, 1957.

Attending psychiatrist, Hillside Hospital; Clinical Assistant Professor of Psychiatry, Division of Psychoanalytic Education, University of New York College of Medicine, New York (Dr. Tarachow). Research Assistant in Psychology, Hillside Hospital (Dr. Korin). Resident Psychiatrist, Hillside Hospital (Dr. Friedman).

various degrees of breakdown of the fused ambivalence, with greater or smaller degrees of pathological expression of the impulses no longer tempered by their opposites. In instances of the complete breakdown of the fusion of the opposing tendencies, one would be dealing with psychosis or extremes of psychopathy, like murder. In neurosis there are various degrees of disturbance of the fusion.

In clinical psychiatry the concept of ambivalence simply refers to the conscious presence of opposing impulses and feelings at the same time. In psychoanalytic theory, though, the problem of ambivalence refers to the unconscious fusion of the opposing impulses, as well as to the varying degrees of breakdown of the fusion. Although this study does not utilize psychoanalytic techniques and is based upon conscious data, the work is with reference to the larger frame of reference toward ambivalence. The total study is in terms of the psychoanalytic frame of reference about the problem.

Method

The structured interview elicits mainly conscious aspects of ego functioning. Such an interview can elicit such matters as conscious indecision, coexistence of opposites, and organization or disorganization of the ego in carrying out its wishes and needs. However, other means can be devised to get more than these conscious evidences of disorganization; it should be possible to get closer to the derivatives of the breakdown of the ambivalent fusion, and even some estimate of the extent of the unconscious breakdown and liberation of the impulses themselves. Other measures, such as the TAT, as a projective test, might give more direct, basic measurements of the opposing impulses. A dot comparison test which has been developed might also give some important measurements. In preliminary correlations these various tests do significantly correlate with one another. However, we shall return to the two tests which concern us in this paper: the interview, and the perception and imagery experiment.

Questionnaire

In the interview, we elicit conscious attitudes centering about certain clusters of information subsumed according to psychoanalytic theory. These questions, presented in an interview and recorded verbatim, are as follows:

A. Introductory Questions
   1. Do you like Hillside Hospital?
   2. Do you like your doctor?
   3. Do you know many of the patients?
   4. Do you like any of these other patients?

B. Orally Derived Attitudes
   1. Do you like to eat?
   2. What is your favorite food?
   3. Are you an optimist or a pessimist (hypothetical example given)?
   4. At a party, are you more apt to be an active talker and participate, or are you more apt to listen?
   5. If you are spending a quiet evening at home, what are you more apt to do—read a book or watch TV?
   6. If you need a moderately important article, do you decide what you want, how much you spend, and then shop for it; or are you more likely to see something in a store window and buy it on the spur of the moment?

C. Anally Derived Attitudes
   1. Are you orderly or disorderly at home?
   2. Do you have trouble making up your mind?
   3. Do you like jokes? Do you like sexual jokes? Can you tell them as well as listen to them? Can you tell them as well in mixed company as you can in a group of women (men)?
   4. Do you believe that children should be brought up with great leniency or with a firm control? Do you believe in the "spare the rod and spoil the child" adage?
   5. If you have made up your mind about something, can you listen if others try to talk you out of it? Have you been called stubborn?
   6. Are you interested in money?
   7. Do you save money?
   8. Do you keep a budget? (If so) do you find yourself running short at the end of the week, or can you keep within the budget?

D. Genitally Derived Attitudes
   1. Who is your favorite actress (actor)?
   2. Have you been in love?
   3. Do you believe in love?
   4. Which of your parents are you most like?

5. Just in terms of body beauty, which would you consider more attractive, a beautiful woman or a handsome man?

E. General Ego Attitudes
1. Do you like to work? What sort of work?
2. What are your major life interests? Do you have any hobbies? If you had your life to live over again, what would you do?

F. Attitudes Toward Aggression
1. If you saw two friends in an argument, what would you be more apt to do—join in or avoid it?
2. What is your attitude toward capital punishment?

G. Attitudes Toward Own Sickness and Therapy
1. Do you think you are sick?
2. Do you think you've come to the right place for help?

The interview was rated for degree of opposites and uncertainties in the following manner: If, in response to any of the questions, conflicting feelings, indecisions, or simultaneous opposite attitudes were expressed, this response was given a score of 1. All other responses were scored as zero. The subjects were classified into three groups according to the severity of disturbance.

Degree of Clinical Ambivalence	Total Interview Score
1. Mild	0-3
2. Moderate	4-6
3. Severe	7 or higher

Some examples of scoring are as follows: In response to the question "Do you like your doctor?" the answers and their scores are noted.

1. "Yes, he's a wonderful person." Score, 0
2. "No, I don't think he understands me or is helping me." Score, 0
3. "As a person, he's very nice——as a doctor . . .? I don't know; he tries, but I'm not sure whether he's doing me any good." Score, 1

Perception-Imagery Experiment

The other measurement, the perception experiment, is simply a variant of an experiment performed by Poetzl [1] in 1917. Variations of this experiment have been performed since by Malamud,[2] Malamud and Linder,[3] and Allers and Teler,[4] and more recently by Fisher,[5,6] in New York, and Luborsky and Shevrin,[7] in Topeka. Poetzl's basic experiment was to present a picture to his subjects by means of a tachistoscope and have them draw what they had seen. This was generally some fractional aspect of the complete picture. If the subject dreamed the following night, he was asked to make drawings of his dream. This often demonstrated that the dream contained portions of the experimentally exposed picture which the subject had not been able to see consciously on the initial exposure. In other words, there was preconscious perception, below the level of consciousness, but which was able to present itself via the dream contents. The experiment carried out in the present study is the modification performed by Fisher. In this variant the subject is shown a picture for $\frac{1}{100}$ second and asked to make a drawing. After this first drawing is made, he is instructed to shut his eyes and await whatever visual imagery might present itself to him at that moment. As soon as the subject was aware of a visual image, he was asked to describe it and make another drawing. This was then repeated up to 5 or 6 times, and by Fisher up to 20 times or more.

This experiment demonstrates the existence of extremely rapid preconscious perception and the speed with which these preconscious percepts are subjected to the primary process, yielding distortions, symbolizations, or various defenses against the perception. Fisher felt that the train of associations stimulated by the test picture is in the grip of the original percept, and that all succeeding imagery represents the percept, its distortions, or the defenses against it. Fisher used dreams in his earlier experiments, but he found that the immediate images in the waking state served the same purpose.

Fisher's data carry with them certain unanswered questions and implications. There is no indication of the percentage of his unsuccessful experiments, nor is there any systematic indication of the personality structures of the subjects. While Fisher's work is lucid and brilliant in exposition, extension of his studies in the areas noted might lead to further conclusions relating to variations in mental functioning and to the factors which might influence such variations.

One such extension was carried out by Luborsky and Shevrin. They studied the

different styles individuals have of incorporating the test picture as day residue into their dreams. They expected these styles to be related to the typical defensive ego operations of the subjects, and their work confirmed their expectations. The factors they believe will affect perception are (1) cognitive style, (2) defensive activity, and (3) states of consciousness.

Against the background of these previous studies, the purpose of this investigation is to determine how the varying fates of the fusion of ambivalence will affect perception and imagery. The hypothesis is that variations in the defensive and synthetic functioning of the ego and variations in the degree of breakdown of the fusion of ambivalence should be reflected in differences in tachistoscopic perception and differences in the quantity and nature of the imagery. The greater the breakdown, the wider the range of imagery. Linn, in his paper on the discriminating function of the ego,[9] makes the point that the ego perceives only that which it can tolerate, and that in the very process of perception there is a selective process of acceptance and rejection within the cluster of meanings associated with every percept. This discriminating and selective process is an ego function. The cluster of meanings can be quite wide, and, according to Kris and Kaplan,[8] include the opposite. A defect or disorganization of ego functioning would interfere with the ego's ability to defend itself against traumatic perceptions, and at the same time extend the range of selections within a cluster of related meanings. This could be expected if the defensive and integrative functions fail. This was the working expectation in our present study. The total range and breadth of the imagery, and not simply the degree of recovery of preconscious perception, are of interest in this study. These variables may give some measure of the breakdown of the ambivalence. It is necessary to know how close the interview dealing with conscious attitudes is to any other measurement which might be closer to the unconscious, to the breakdown of the ambivalent fusion, and the measurements of the freed and contradictory impulses and feelings. It is precisely for this reason that the breadth and range of the imagery are of such interest. One important difference from Fisher's technique was the use of a scene of violent battle, as compared with neutral pictures used by him. While the purpose in the imagery experiment was chiefly to study the range of imagery, perhaps the study could also serve as a partial control to these variations of the Poetzl experiment, just as Luborsky and Shevrin's work serves as a partial control. These authors have already indicated that defensive and cognitive style influences the utiliza-

Fig. 1.—Medieval scene of violent battle.

tion of preconscious perception in dreams and imagery.

The study is based on 29 subjects, using psychoneurotic inpatients or outpatients at Hillside Hospital. Psychotics, psychopaths, patients with behavior disorders, and adolescents were not used. The mean ages of all three groups were the same, approximately 32 years. There was no significant difference in the level of education.

The picture used is a medieval scene of violent battle (Fig. 1). The soldier facing the viewer has just delivered a powerful blow to another. The latter soldier is falling backward. The sword is up and to the right. The background is a wooded scene with water underfoot. To the left the water is in some agitation. This picture was exposed for 1/100 second and we searched for perception and imagery as described below.

The data were studied under the following subheadings and using the scoring criteria noted.

1. Correctness of perception of aggression at original exposure
   Scoring criteria—Perception of a fight scene or perception of implicit aggression, such as a man chopping down a tree or holding a weapon
2. Correctness of perception of sex at original exposure
   Scoring criteria—Both figures are perceived as male
3. Imagery reproduction in all the subsequent drawings with regard to three variables
   (*a*) Human qualities
   Scoring criteria—The criteria for this and the following variables were difficult to establish because of the number of factors involved and the wide range of possibilities within each factor. In each case, one of us scored each set of images and the other two later scored them independently. The scores were then compared and discussed. In each case, scoring was done without any knowledge of the degree of ambivalence that was present, as determined by the questionnaire. For human qualities, scoring factors included the presence or absence of images containing humans and the degree of life-like representation, including pose, fluidity of lines, etc.
   In the above and in the two succeeding factors, each set of images was scored as poor, fair, good, or very good.
   (*b*) Detail
   Scoring criteria—The amount of detail involved in all the drawings, whether of humans or inanimate objects. For drawings of humans, facial features, the absence of "stick-figures," clothing details, etc., were the major criteria.
   (*c*) Affect and motion
   Scoring criteria—The expression of affect or motion, either in the drawing itself or in the verbal description, was the crucial factor. The presence and degree of pain, happiness, flight, fear, aggression, etc., that were expressed were used as a basis for the score.

Examples of the application of the above scoring criteria follow:

Figure	Human Qualities	Detail	Affect and Motion
2	Good	Fair	Good
3	Poor	Poor	Poor
4	Fair	Poor to fair	Fair
5	Good	Good	Very good

4. Degree of recovery of preconscious percepts
   Scoring criteria—The stimulus picture contains a warrior swinging a sword, a warrior stunned by the sword, a body of water to the lower right, a body of agitated water to the lower left, and a background of trees and bushes. The presence of any of the above factors in the imagery was considered to indicate some recovery of preconscious percepts, provided that they had not been seen on original exposure. For example, Subject J saw the two fighting figures in fine detail (Fig. 6) but saw none of the other elements of the picture. In one of his images (Fig. 5), he saw a body of water in the lower right-hand corner and a few trees in the back-

Fig. 2.—Patient 32. Drawing of Medieval scene (Fig. 1). Severe impairment of ambivalent fusion.

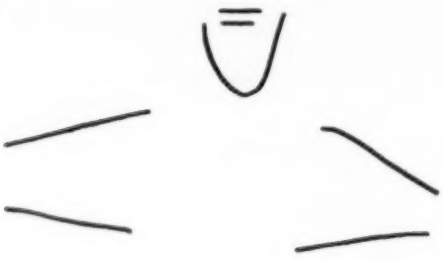

Fig. 3.—Patient 27. Medieval scene (Fig. 1). Slight impairment of ambivalent fusion.

Fig. 4.—Patient 19. Slight impairment of ambivalent fusion.

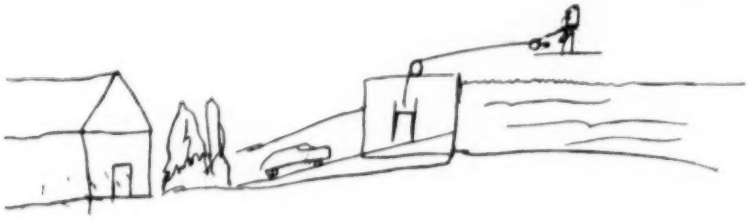

Fig. 5.—Patient J. Image No. 2. Severe impairment of ambivalent fusion.

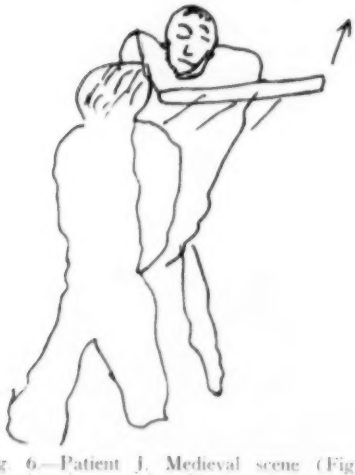

Fig. 6.—Patient J. Medieval scene (Fig. 1). Severe impairment of ambivalent fusion.

ground. Further, the image revolved around a fantasy in which the drawn figure would pull up the sluice gate and send a torrent of water over the lower left side of the drawing. This image was scored as showing some degree of recovery of preconscious percepts.

5. Over-all breadth and range of imagery

Scoring criteria—Scoring was based on the number of different themes, subjects, ages, affects, sexes, etc., that was evoked by the imagery and was a simple numerical tally. It was carried out under the headings: no range, slight range, moderate range, and wide range. For example, a subject who had three images, each of a different hospital doctor sitting at his desk, received the score of "no range"; another subject's imagery evoked scenes of battle, of a mother playing with her children, and of the hospital grounds with patients walking. This subject's imagery received the score of "wide range."

Results

1. *Correctness of Perception of Aggression*

Severe group	perceived well to excellent	in 5 of 11	45%
Moderate	perceived well	in 2 of 8	25%
Low	perceived well	in 1 of 10	10%

The differences between proportions are not statistically significant at the 5% level of confidence, but they approach this level of significance (Table).

Relation Between Degree of Ambivalence and Factors of Perception and Imagery

Factor	Degree of Ambivalence			Difference Between High and Low Groups, %	Critical Ratio	Significance of Difference
	High N=11	Moderate N=8	Mild N=10			
1. Correct percept of aggression	45%	25%	10%	35	1.75	Not significant $P>5\%$
2. Correct perception of sex	72%	50%	40%	32	1.45	Not significant $P>5\%$
3. Human qualities—good or better	63%	0%	0%	63	3.15	$P<1\%$
4. Detail—good or better	36%	37%	0%	36	2.40	$P<5\%$
5. Affect and motion—good or better	63%	0%	0%	63	3.15	$P<1\%$
6. Good or better recovery of preconscious percepts	82%	75%	30%	52	2.36	$P<5\%$
7. Moderate or better range of imagery	72%	38%	10%	62	2.86	$P<1\%$

2. *Correctness of Perception of Sex*

Severe group	perceived correctly in 8 of 11	72%
Moderate	perceived correctly in 4 of 8	50%
Low	perceived correctly in 4 of 10	40%

The differences between proportions are not statistically significant at the 5% level of confidence, but they approach this level.

3. *Drawings, Human Quality*

Severe group	very good and good in 7 of 11	63%
Moderate	good in 0 of 8	0%
Low	good in 0 of 10	0%

The difference between the severe and the low group is significant at the 1% level of confidence. That between the severe and the moderate group is significant at the 5% level of confidence.

4. *Drawings, Detail*

Severe group	good in 4 of 11	36%
Moderate	good in 3 of 8	37%
Low	good in 0 of 10	0%

The differences between the severe and the low group and between the moderate and the low group are significant at the 5% level of confidence.

5. *Drawings, Affective Quality*

Severe group	good in 7 of 11	63%
Moderate	good in 0 of 8	0%
Low	good in 0 of 10	0%

The difference between the severe and the low group is significant at the 1% level of confidence. The difference between the severe and the moderate group is significant at the 5% level of confidence.

6. *Recovery of Preconscious Percepts*

Severe group	Some recovery of any degree in 9 of 11	82%
Moderate	Some recovery of any degree in 6 of 8	75%
Low	Some recovery of any degree in 3 of 10	30%

The difference between the severe and the low group is significant at the 5% level of confidence.

7. *Over-all General Range of Imagery*

Severe group	Moderate to wide in 8 of 11	73%
Moderate	Moderate to wide in 3 of 8	38%
Low	Moderate to wide in 1 of 10; no range in 3	10%

The difference between the severe and the low group is significant at the 1% level of confidence.

The data show a consistent pattern. As compared with the low group, the severe group shows (1) more correct perception of aggression, though not of statistical significance; (2) more correct perception of sex, though not of statistical significance; (3) better human quality in the drawings; (4) better detail in the drawings; (5) better affective quality in the drawings; (6) better recovery of preconscious percepts, and (7) wider range of imagery.

Comment

We feel that our data support our working hypothesis. The data may not all be statistically significant, but the evidence is moving in the right direction. The patients classified as high in our interview are those subjects whose integrative and defensive ego functioning is poorest and, according to our working idea, is closest to impairment of the fusion of ambivalence. These are the subjects who would be less able to defend themselves against the disturbing qualities of a stimulus picture. Further, in view of the impaired defensive functioning in these persons, the cluster of associations and related imagery should be wider in this group. Our data indicate that this is so. Further theoretical basis for this will be adduced below. Where ego functioning is poorer, there should be a greater accessibility of preconscious material. Our over-all working notion is that this state is also connected with a greater degree of disturbance of the fusion of ambivalent tendencies.

Our subjects classified as low on our interview really fall into two groups. In one the choice of attitudes seemed relatively relaxed, while in the other the subjects seemed to be highly defended, compulsive characters whose responses were all organized in one direction, but in a rigid, compulsive manner. Both these groups were classed as low. Clinically, our assumption is that these rigid compulsive characters have erected strong defenses against one side of their ambivalence, and that there is substantial disturbance of the ambivalence. In our low group there is much more active and stringent defensive functioning than in the high group, even though in some subjects this defensive functioning is not healthy and in the nature of reaction formations.

Linn,[9] in a discussion dealing with the discriminating function of the ego, suggests the notion that the ego perceives only that which it can tolerate, and that in the very process of perception there is a selective process of acceptance and rejection within the cluster of meanings associated with every percept. This process of selection depends on the psychic structure of the subject as well as the organic integrity of the brain. It also depends on the anxiety-provoking characteristics of the stimulus. Linn developed this cluster concept from an idea of Kris and Kaplan.[8] Kris and Kaplan discussed the wide range of ambiguity surrounding any percept. According to them, this range includes all varieties of connection, even including the opposite. Both Kris and Kaplan and Freud[10] point to the identity of opposites in the sense of the antithetical sense of primal words. Following this reasoning, the range of ambiguity about any percept must include its opposite; and words, sensations and feelings are all relative. Kris[11] has expressed the opinion that tachistoscopic perception is more liable to dissolve percepts into all their archaic and ambiguous components than is ordinary vision.

Linn and others point out that the principle of closure (of a Gestalt) is in itself important in affecting perception. There is a certain effort necessary in perception of differences or in traumatic perception. Perception may be imperfect and dominated by the wish to see that which is easiest to see, and dominated by the need to expend as little energy as possible in making the perception.[12] In facing a highly traumatic stimulus, it might be quite compatible with the principle of economy in the expenditure of energy for the ego to seek out a comfortable point in the whole ambivalent range and to be content with the opposite as the

percept. (As shown in Figure 2 the warrior was perceived as a woman.) It might be more comfortable to see aggression as love, a warrior as a doctor. This latter occurred quite often in our subjects. Hartmann,[13] too, in discussing Poetzl's work, as well as his own experimental work, makes the point that preconsciously perceived stimuli in the tachistoscopic experiment represent the drive to closure, the need to expend the energy stimulated. A traumatic picture, such as we used, creates a drive to closure; a process akin to the repetition compulsion is set up. The appearance of the opposite in the place of the true percept might represent several factors. Important among these factors is the discharge of energy displaced from one point to another in the ambiguous range of related percepts—or, the greater the need for defense the farther away from the true percept.

The question, of course, might be raised as to what our questionnaire actually does reveal—does it measure degrees of breakdown of fused ambivalence, as we assume? Our classifications were made not on the basis of clinical judgment or diagnosis but on the basis of the questionnaire. Our interview was carefully limited to the questions, and we avoided knowledge of the clinical diagnosis until after all the data were gathered. We might repeat that this present study presents only a limited part of our data. Each subject is given a visual dot comparison test, a TAT adapted to our purposes, and the Szondi test, all to determine the degree of ambivalence. We find a positive correlation of all these tests. The total data are to be reported subsequently. After our data were complete, we compared our three groups as to clinical diagnosis. There does not seem to be any correlation with clinical categories.

A further investigation into our data which we are now carrying out is a division of our group classified as low into two groups, one a compulsively defended group and the other a more relaxed group. We are investigating whether these two separate subdivisions will present contrary etiological configurations, different performances on the tests, particularly whether they behave differently in the perception and imagery experiment. We are enlarging our sample and are not yet prepared to present these results. Another set of data which we are in the process of correlating is the estimate of the patient's ambivalence made by the psychotherapist and the classification on our questionnaire.

In discussions with colleagues, other possibilities have been raised to explain the greater range of imagery in the severe group. It has been suggested that this is clinically the sickest group, the most frustrated, and the group which therefore has the greatest recourse to fantasy gratifications; it has also been suggested that it is the healthiest group, with the greatest flexibility, capacity, and tolerance for opposing types of material and affects to be permitted entry into consciousness. Our own view is as stated, that this impairment is a function of impaired integrative and defensive ego functioning. Our own present response to all these suppositions, including our own, is to note that the high group does not show less or more psychopathology than the other groups when examined from the clinical standpoint. One of the steps we are contemplating is a separation of all our data on the basis of clinical categories, to see how they would behave perceptually and in our other tests. In a previous study by Tarachow and Fink [14] patient material was divided into clinical categories and correlated with etiological factors, specifically object loss, with results that were statistically reliable. However, this group was not subjected to any of these experimental procedures.

Summary

Our data suggest that differences in ego organization do have an effect on performance in tachistoscopic experiments, especially in the elicitation of subsequent imagery. If the trend can be maintained by further data, it would be of real interest. The patient with some disturbance in the ambivalent

fusion is closer to his preconscious. Certain aspects of his ego functioning permit or force him to be in closer contact with all his impulses: His defensive functioning is less efficient. The reward for this ego deficiency might be greater perceptiveness, greater emotionality, and, perhaps, greater imagination and creativeness. The less well-defended personality might be more sensitive to selective aspects of reality. Ego defenses not only keep our internal affairs under control and in check but also interfere with our perception of reality. Overly strong ego defenses might estrange us not only from our inner life but from reality as well.

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A Prognostic Indicator of Treatment Failure in Schizophrenia

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Introduction

In the population of any large mental hospital one frequently encounters patients diagnosed according to one of the typical nosological classifications of schizophrenia who, in spite of numerous therapeutic efforts on the part of medical personnel, maintain a stationary clinical course. Such patients neither regress to a more primitive state nor show any appreciable improvement during extensive periods of interrupted or continuous hospitalization. Although they display few, if any, regressive phenomena in the integration of their thinking, they can adjust adequately only to benign environments, a fact that is readily apparent from the frequency of their readmissions. These patients are resentful of hospitalization, claim they are not mentally sick, and seem from the beginning to have and maintain a negativistic attitude toward any attempts at treatment. Since the families of such patients have tremendous difficulty in coping with the patients' usual bizarre modes of living, they exert a great deal of pressure for the initiation of all conceivable types of psychiatric treatment within the hospital setting. At the same time, the reluctance of the patients themselves for continued hospital care creates a vicious circle which first plays the patient against the family and eventually against any therapeutic program offered by the hospital.

As a result of years of unsuccessful treatment efforts with such cases, many a mental hospital psychiatrist has wondered in retrospect how he was ever maneuvered into attempting so much treatment where failure was the inevitable outcome. Such therapeutic quandaries could perhaps be avoided if we were able to sharpen our prognostic criteria along the lines so aptly described by Bleuler,[1] in which he postulates both an "extent prognosis" and a "direction prognosis":

> Within the realm of schizophrenia there are again different directions such as the paranoid, catatonic, dementia, etc., that have to be considered in the prognosis. Not less important is often the "extent prognosis," i. e., the prediction how far the disease will progress within a conceivable period. Will the disease soon come to a stop, or will there be some improvement? Will the patient become socially incompetent through dementia? Or will he be able to maintain himself in spite of the disease? And under what circumstances?

If it were at all possible to develop prognostic criteria for the "direction" and the "extent" of schizophrenic reaction types on the basis of longitudinal studies, the chances of falling into a "therapeutic trap" or "therapeutic cul-de-sac" would be less. Not only would valuable time and effort be saved and be directed toward more fruitful therapeutic endeavors, but the frustrating entanglements with many of the type of patients described above could be avoided. The development of such prognostic criteria is one aspect with which this paper is concerned. However, there is

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another, related aspect which must, of necessity, receive detailed consideration. This has to do with the concept of "change." The implication of what constitutes "change" in describing a course of therapy (whether it be for the better or the worse) is essentially an inherent problem and in need of further exploration.

Theoretical Considerations Regarding the Concept of "Change" in Mental Illness

In evaluating the effects of any therapeutic intervention, be it therapy within a psychoanalytical frame of reference, therapy through pharmacological shock or ataractic drugs, or the many therapeutic approaches which might be employed, criteria for determining "change" are essential. Too often the real issue at hand is neglected—how indicative of a basic personality change are the criteria that we use in measuring the effects of a therapeutic program?

In respect to this problem our thinking often becomes muddled, with value judgments stemming from an overconcern with whether a patient appears outwardly to be "sicker" or "healthier" after a course of therapy. Quite evidently we do not take consideration of the fact that criteria for "change" are not necessarily interchangeable with the criteria for "improvement," which are highly weighted with social-value concepts. In such criteria a great amount of ambiguity results, depending upon who defines improvement—the patient, the therapist, or the patient's family. Consequently, unless we measure "change" during therapy within a well-defined framework of personality structure, we are prone to get involved in the ambiguous issue of what constitutes improvement. Any valid description of "change" should include a consideration of those changes in ego functioning that are occurring at any point during a therapeutic course. What ego strengths appear or diminish in their intensity? What are the more serious ego regressions that are relinquished in lieu of reinstituted defenses, and what are their total effects upon the personality structure?

A Proposed Method for Studying "Change" in Schizophrenic Patients

The theoretical basis of this proposed method for evaluating change began with a series of investigations into the problem of schizophrenia conducted by Beck[2] as the principal investigator and reported in his monograph "The Six Schizophrenias." These investigations have provided a description of schizophrenic reaction types within a conceptual schema of personality structure incorporating five theoretical components: (*a*) defensive organization; (*b*) associational integration; (*c*) fantasy activity; (*d*) emotional state, and (*e*) social adaptation. Also included in this schema are the levels at which these components occur in each of the respective schizophrenic reaction types (Appendix A, Table 1).

In order to obtain the above personality components, operational statements which comprised a trait sample of 120 items descriptive of behavior were subjected to a factor analysis within the framework of Stephenson's Q-technique. Since the publication of Beck's monograph, an additional 50 traits have been added, increasing the trait sample to 170 items. The additional 50 items include descriptions of behavior which apply to "normals," as well as other clinical groups, rather than to schizophrenics alone. The resulting trait sample can be applied to all levels of personality integration, extending along a broad continuum from the hypothetical "normal" to those severely disruptive ego functions typical of the classical schizophrenic process. Rorschach correlates for each of the 170 items of behavior were then formulated by Beck and Molish.[3,4] A list of these 170 trait items and their respective position in the framework of personality structure described above may be found in Table 1, Appendix A.

The trait items listed in Table 1 may be Q-sorted on the basis of correlates from Rorschach Test records. According to the

traditional methodology of Stephenson's Q-technique,[5] the rated degree of characterization and the frequency of items for each rating are divided into 13 steps to achieve a quasinormal distribution of judgments, with small gradations from one rating to the next. The criteria for rating a trait as characteristic or not may be judged by the presence or absence of the Rorschach correlate for the particular trait in question, as determined in any particular Rorschach record. The middle of the 13-step continuum (Levels 5, 6, and 7) is used for those traits which did not characterize the patient to any great extent. Traits rated from 8 to 12 are considered as definitely characteristic, while those rated from 0 to 4 are regarded as not being characteristic. No trait itself is considered out of context of the personality as a whole. When any one trait is rated as highly characteristic, we are making a quantitative judgment as to where it belongs on the 13-point scale in relation to the degree of importance it has for that personality structure as compared with other traits. A qualitative judgment is, of course, involved in this interitem comparison.

It is entirely possible that through the use of the Rorschach Test within the framework of personality structure and methodology described here one can obtain critical measures of "change" during courses of therapy. The change of ego functioning within every area of personality structure can be described, both within each of the four components of personality and within the total functioning of the personality structure, which is reflected in the degree of characterization of those traits dealing with social adaptation. Also, by such a framework of reference within which change is measured one avoids becoming muddled with the ambiguous criteria already referred to.

It is within this theoretical framework that we have directed our efforts toward evaluating the changes in various ego functions in the personality structure of one schizophrenic patient as they occurred during a lengthy period of hospitalization. In order to do this, the 170 trait items in Table 1 were Q-sorted for each of three Rorschach records for this patient. The resulting ratings (with a possible range of 0 to 13) for each item for each of the three testings are shown on the extreme right of the Table. As described earlier, the criteria for rating a trait as characteristic or not were judged by the presence or absence of the Rorschach correlate for that particular trait as determined in each of the three Rorschach records.

We plan to demonstrate how the three Rorschach Test records, evaluated on the basis of the described methodology, point out the status of the various ego functions at three respective intervals during this patient's course of therapy. In addition, we hope to show that if the course of treatment in this one patient had been directed and modified when indicated, in accordance with the longitudinal Rorschach findings, much time and effort would have been spared and the eventual "therapeutic trap" avoided.

The Patient in the Therapeutic Maze

Patient A had her first contact with a psychiatrist at age 14. At age 18 she was hospitalized for two months in a private psychiatric hospital. From then until the age of 21 she was seen by private psychiatrist, from whom she received psychotherapy. At age 21 she was admitted to a state mental hospital and again received psychotherapy, for almost a year and one-half. This attempt also failed, and she was started on insulin coma therapy, which was later combined with electric shock. However, in spite of all these efforts, the patient's status remained unchanged. When the ataractic drugs were first introduced into the hospital, in May, 1954, she was promptly placed on them, and over a period of a year or two she received prolonged trials of alternate treatment with chlorpromazine, placebo, and reserpine. To these she showed no particular response. Finally, a prefrontal lobotomy was performed, and again she seemed essentially unchanged. Shortly after her lobotomy, because she seemed more antagonistic than ever, she was placed on chlorpromazine. Following several months of this drug treatment, only a minimal diminution of her symptoms was noted.

A log of the patient's treatment experiences is presented in Appendix A, Table 2, and a detailed summary of her history in Appendix B. This history was obtained from an analysis of hospital records, from interviews with personnel involved in the treatment of the patient (including the patient's psychotherapist in the hospital), and, finally, from interviews with the patient herself.

The Preinsulin Personality Structure as Evaluated by the Rorschach Test

Just prior to the initiation of insulin coma therapy the patient was administered Rorschach Test I (March 27, 1953). At the time of this testing she was one of a group of patients on whom the effects of insulin coma therapy were being studied. The Rorschach Test was administered, scored, and Q-sorted by one of us (H. B. M.). The method followed was that described in detail above.

A list of ratings for each of the 170 personality traits within a conceptual schema of personality structure for Rorschach I will be found in Table 1 (Appendix A). The following is a description of the personality structure according to the five components of personality: defenses, associational integration, fantasy activity, emotional state, and social adaptation, and the levels at which they are manifested.

Defenses.—It is evident from the ratings of the various traits representing defenses as evaluated by Rorschach I that the maneuvers which reflect hyperrepression are emphasized. Thinking is inhibited and blocked; breadth of interest is narrowed, as well as attention. The intrapsychic constriction is further noted by the repression of fantasy activity and the avoidance of affects. With much of the inner psychic force blocked out, the result is, in general, a barren personality structure. The vulnerability of these defensive strategies is, however, emphasized by the fact that the hold on reality is not a rigid one. The constrictive aspects of the defenses enable the patient to exercise a rigid hold on the self, but fail to allow her to maintain a rigid hold on reality. The defenses are therefore brittle in nature, and the telltale signs of their incipient crumbling are noted. In this respect, the mechanism of projection as a pathogenic defense for this patient is of interest, and the rating of 8 in this first Rorschach test indicates the latency of possible paranoid ideation.

Associational Integration.—In this area of personality structure, the most characteristic trait items are actually the exact antithesis of what one would expect for schizophrenic behavior. Thinking is purposeful; language productions are orderly; thought is logical, as well as coherent, and the abstract attitude is not seriously impaired. However, although no regressive phenomena typical of the classical schizophrenic thought disturbance are noted, some losses of ego functioning in this component of the personality are noted. The ability to attend and concentrate adequately is doubtful (rated as 7). Reality testing itself is deficient (inadequate reality testing, rated as 8). Associated with this is the patient's proneness to use vague analogies and commit logical blunders in judgment. In addition, a suspicious note of indifference pervades the attention span. (Attention is indifferent to point of apathy, rated as 7). The deficient regard for reality is not a result of actual distortion, but is a function of indifference and lack of critical attention. The F-responses in the Rorschach record itself are impersonal in nature and not bizarre, unique, or regressive.

Fantasy Activity.—The effect of this patient's constrictive defenses is reflected in the dearth of fantasy activity. The patient represses any self-gratification attained from fantasy living. Traits indicative of fantasy activity are rated with a minimal degree of characterization. Some fantasy is noted, but it is weakly experienced, passive, or static in stance and offers little gratification. The fantasy living in general is not indicative of any really creative imagination, and, in view of the hyperrepression, it is not effectively integrated into the total personality structure. As regards the schizophrenic process itself, the fantasy life reveals no regressive

features. This is to be expected within the framework of the intrapsychic constriction described, since the fantasy that is noted offers little or no gratification of any type. Certainly, this patient does not take recourse to fantasy living in an attempt to seek solution for conflict.

Emotional State.—As constricted as this patient may be, the affective tone is not one of apathy, as one might expect. Lability characterizes the affective reactions. The patient is described as irritable and impulsive, and the over-all control over basic drives is minimal. The labile nature of this affect indicates that many of the constrictive defenses are aimed toward constraining such affect. With a minimum amount of fantasy living resorted to, the threat of this potential emotional explosiveness is even intensified. Thus, against an overt picture of blandness at times, there is a continual unrest. The patient's mood continuum can vascillate, at times becoming excited, with a lack of control exerted over the distribution of energy. The affective nuances then dominate the thinking. The brittleness of the described constrictive defenses is noted by the fact that this labile affect certainly breaks through the rigid barrier and can at times eventuate in acting-out behavior (tantrums, and aggressive, self-assertive outbursts, rated as 10). This same level of feeling tone predominates over the entire personality structure, and a wider variety of emotional expression found among normals is lacking. Thus, it is not possible for the patient to attain any controlled release of her emotions. The patient is unable to give vent to her feelings without anxiety or to display spontaneous affect with any degree of control. The result is a lack of order in the change of one emotion to another, which enables us to see the patient now as rather flat, and in the next moment as irritable and agitated.

Social Adaptation.—The nature of the schizophrenic process in this patient is readily perceptible in the level at which she adapts socially. Many traits characteristic of self-deprivation are noted. The unbearable environment is warded off by a hard, encapsulated shell in which she lives from day to day. Excessive repression, low level of aspiration, narrowing of interests, and cramped and rigid attitudes highlight this self-deprivation. Intellectual efficiency and achievement potentials are narrowed. Everything pleasurable appears to be repressed, as well as the potentials for learning and enjoyment. The patient withdraws from social activity or, in the least, cannot participate adequately in interpersonal relationships. The environment is rejected; change is resisted, and the environment is regarded in an indifferent fashion. The environment is accepted only when it conforms to the encapsulated structure within which the patient reacts. Emotional rapport with and understanding of others are lacking. The self-deprived and self-absorbed nature of her social adaptation is emphasized by the fact that few traits depicting constructive life objectives are noted.

The Postinsulin Personality Structure as Evaluated by the Rorschach Test

In April, 1953, the patient was started on insulin coma therapy and had received a total of 48 insulin treatments by June 5, 1953. During the course of her insulin treatments she had 36 comas, together with 5 electric shock treatments. The nursing notes during this period describe her as cooperative, and quite frequently she awakened from her coma in a friendly, smiling mood, with the question: "Why can't I go home—I'm not crazy." Occasionally she would be sullen and demanding. A cyclical phenomenon of friendliness and sulleness continued throughout her course of treatment. None of the nursing notes describe her as being particularly disturbed, and her contact remained good. After her insulin was terminated, the patient's status was considered to have undergone slight improvement. She was given her second Rorschach test at the termination of treatment.

In spite of the intervening insulin coma and electroconvulsive therapies between Rorschach I and Rorschach II, there is little change noted in the over-all personality structure as evaluated by the new Rorschach record. The high correlation of 0.73 between the Q-sort ratings from Rorschach I and Rorschach II, shown in Table 3 (Appendix A), indicates the limited degree of change in the patient's basic personality pattern. For a more qualitative analysis of the personality structure as evaluated at the time of Rorschach II, we again refer to Table 1, which lists the Q-sort ratings for Rorschach I and Rorschach II. By comparing these ratings, we are able to evaluate the qualitative aspects of change as they appear throughout the various components of personality structure.

Defenses.—The defensive strategy shows no change from that evaluated in the first Rorschach record. If anything, there has been some intensification of the repression as noted in the comparative ratings for Trait 151. Affects are avoided or blocked off. This trait is highly characteristic at the time of Rorschach II*. In conjunction with this evidence for constriction, there has been an over-all increase in the suppression of aggression.

Associational Integration.—The only noted change in this area of personality structure is in relation to the level of reality testing. At the time of Rorschach II, Trait 125, "adequate reality testing," is rated as 7, compared with a rating of 4 for Rorschach I (F+% Rorschach I=50; Rorschach II, F+%=62†). Thus, at the time of Rorschach II a trend toward a healthier regard for reality testing is noted. Concomitant with this trend is the patient's increased ability to concentrate (Trait 126, "able to concentrate").

Fantasy Activity.—There are few, if any, qualitative changes noted in this personality component. Consistent with the trend toward a more adequate level of reality testing, there is some increase in the patient's ability to control daydream activity; i. e., the fantasy themes are less autistic and unique (Trait 55). Yet this is merely a trend toward improvement when we consider the integration of the fantasy living into the entire functioning personality structure. The fantasy themes are still rather monotopical; the over-all fantasy activity is not well integrated with the social and emotional life, and it is not really creative. The fantasy role still lacks real verve and direction in being a recourse in seeking solutions for, and working out real life problems.

Emotional State.—With the increased repression noted in this area, there has been a consistent decrement in the over-all emotional instability noted at the time of Rorschach I. The affect no longer may be regarded as labile. The majority of those traits listed in Table 1 under Section IV A (Emotional State, Lability) are no longer considered as characteristic of the patient's affective status. The most noted decline is in the over-all reduction in the lowered threshold of irritability. The mood has toned down from its level of excitement, and the propensity for tantrums and aggressive outbursts has declined. General unrest and strong and anxious affects no longer predominate the emotional state. Affect no longer dominates the thought processes. However, the latency of hypersensitivity and uncontrolled energy distribution still reflects the results of "clamping down the lid" on the emotional lability noted at the time of Rorschach I. The over-all result of such affective control is a costly one and has resulted in too great a reduction of emotional life. The ego thus has suffered notable losses in this area of personality structure. The affect now is much too

* Sum C=4.0 (CF=4) in Rorschach I, as compared with Sum C=1.0 (CF=1) in Rorschach II. Although these Rorschach factors are important in rating the respective traits referred to, there are additional Rorschach correlates used. The reader is referred to Molish.[8,4]

† Although these Rorschach factors are important in rating the respective traits referred to, there are additional Rorschach correlates used. The reader is referred to Molish.[8,4]

fixed in tone, and sensitivity to outer stimuli is notably reduced. The patient now appears apathetic and torpid in her emotional reactiveness. The over-all emotional impoverishment is emphasized.

Social Adaptation.—Self-deprived level of social adaptation still describes the personality structure at the time of Rorschach II. The increased blocking-out of affect has resulted in an intensification of the patient's withdrawal from adequate social participation. Although she is now more capable of mastering her drives and energies by intellectual control (Table 1, Section V D, Trait 16), this control has been possible only by the patient's encapsulating herself within the brittle defenses of excessive constriction. The resulting level of social adaptation still reflects as much self-deprivation as was noted at the time of Rorschach I.

The Postlobotomy Personality Structure as Evaluated by the Rorschach Test

Although the nursing notes at the termination of the above phase of the patient's treatment indicated a slight improvement, this improvement was of short duration. Once more, an additional "cul-de-sac" was added to the ever-increasing maze of therapeutic approaches. For a period of a year or more, chlorpromazine and reserpine were administered. Again, the patient showed little or no improvement clinically. Finally, the maze of attempted therapies culminated in a prefrontal lobotomy in January, 1956, and once more chlorpromazine was added to the treatment program. In April, 1956, the personality structure was again evaluated by the Rorschach Test.

The relative *status quo* of the personality structure as described by Rorschach II when compared with the findings of Rorschach III is evident in the correlation of 0.88 (Appendix A, Table 3). Again, we must be concerned with evaluating the qualitative aspects of this longitudinal study of personality structure, and we refer once more to the changes in levels of manifestation for the trait items presented in Table 1.

Defenses.—The one marked change in the area of defenses is in relation to Trait 82, "rigid hold on reality." This is a result of the gradual increase in the repression and represents one of the ego losses that result from a chronic encapsulation of the personality structure by intrapsychic contraction. This is a function of the hardened shell by which the patient staves off the ever-threatening and unpleasant environment.

Associational Integration.—Few, if any, changes are noted in the sphere of associational integration. Reality testing is now well within healthy limits (F+% Rorschach III=82). However, in the light of the entire personality structure, this must be regarded as further evidence for the stringent efforts at control. The noted loss of ego functioning which results is the loss of the abstract attitude in the patient's thinking. The thought processes are now regarded as overly concrete.

Fantasy Activity.—No remarkable changes are noted in this personality component. However, the ever-increasing reduction in mental life is reflected in the beginning decrement of recourse to fantasy living (Traits 109 and 139 rated as 7).

Emotional State.—The evidence for the brittleness of the constrictive defense strategies over the affect is aptly demonstrated by the changes in this area of personality structure. The latent irritability, the persistent penchant for impulsivity, begins to show itself again after subsiding (as evaluated at the time of Rorschach II). Thus, excessive irritability, tantrums, general unrest, and hypersensitivity bespeak the loosening of the "tight lid" that was clamped down on the patient's affective life. Still there is no controlled release of emotional reactions. This does not reveal any marked increase in her emotional responsiveness, but is still a function of the undercurrent of irritability. Thus, essentially, the patient appears just as apathetic

and emotionally impoverished as at the time of Rorschach II. However, this entire picture indicates that the defense against unstable emotional reactions is crumbling, and that the irritability noted at the time of Rorschach I is beginning to break through the hardened shell of constriction.

Social Adaptation.—The intensity of the self-deprivation in social adaptation still persists. Withdrawal from social contact is more characteristic and is rated as 12 (Table 1, Section V B, Trait 57). This is not a withdrawal into fantasy living, but one which is a function of the rigid hold over the self and the cramping of attitudes. At the same time, thinking is more impoverished. The patient is now more aware of social canons, and the indifference to reality noted in the two previous Rorschach records no longer exists. However, this latter change has been achieved by an over-all rigidity and an ascetic denial of the self. Emotional rapport is still lacking; there is little investment of affect in social activity, and an over-all anergic attitude prevails.

Comment

A longitudinal Rorschach study of one schizophrenic patient with an extensive period of hospitalization has been presented above. Judging from a complete description of the course of treatment followed, the patient was exposed to all the intricacies of a "therapeutic maze," which apparently culminated in one blind alley after another. It is not our purpose in this paper to criticize the therapeutic program followed, nor is it our contention that such therapeutic blind alleys are unavoidable. We are well aware of the fact that less drastic and more carefully planned therapeutic programs still fail to produce improvements in many patients. Our primary purpose in this paper is to demonstrate the methodology we have proposed, to predict and to measure change in personality structure resulting from therapeutic interventions in terms of a conceptual schema of personality incorporating five basic theoretical components: defenses, associational integration, fantasy activity, emotional state, and social adaptation. The case of a representative schizophrenic patient was selected to demonstrate the applicability of this methodology.

The use of Q-sort ratings in our proposed methodology provides an objective measure of the level of manifestation for each of the 170 trait sample items descriptive of personality. Since correlates have been determined for each item comprising the trait sample, the Rorschach Test record can be used ideally as a means of rating each item in the Q-sort distribtuion. An interview situation may likewise be the basis for judgments regarding the 170 personality trait items, thus enabling a therapist to use the same trait sample to Q-sort the clinical picture presented by patients at any given time of evaluation. Both the Rorschach and the therapist's Q-sorts may be correlated for pre- and post-treatment and quantitative, as well as qualitative, comparisons made for all the components of personality structure. In this way the same criteria are used by both the therapist and the Rorschach Test interpreter in defining change. Also, for diagnostic purposes both sorts may be correlated with the Q-sort distribution of each of the schizophrenic reaction types described by Beck [2] and Molish.[3,4]

In his monograph, "The Six Schizophrenias," Beck defines six schizophrenic reaction types, designated as S-1, S-2, S-3, SG, SR-1 and SR-2 (Table 5, Appendix A), in terms of the same conceptual schema of personality structure followed in this paper. Of these six reaction types, our main concern is with Type S-3, since this type best describes the patient in this study. Table 4 in Appendix A lists the correlations of the three Rorschach Q-sorts for the patient currently being studied and the Q-sorts for each of Beck's six schizophrenic reaction types. It is apparent from this Table that our patient consistently correlates to a significant degree with Type S-3 at the time of each Rorschach evalua-

tion. Of interest, also, are the negative correlations with the Types S-1 and S-2, the most classic of the schizophrenic disorders.

The schizophrenic process in the S-3 Reaction Type is characterized by an over-all reduction in mental life. Patients falling within this category live in a hard, encapsulated shell, which wards off a threatening environment. These patients are capable of their own protection and self-care, seldom display regressive psychotic thought, and in a relatively benign environment may even be regarded as fairly well adapted and mindful of social canons. In brief, the personality structure of this type as described within our conceptual schema is as follows: Defenses—constrictive; Associational Integration—orderly; Fantasy Activity—little or none; Emotional State—fixed tone or labile, and Social Adaptation—self-deprived. The more detailed, qualitative aspects of this personality structure can be inferred from our earlier discussions of each of the three Rorschach records.

The importance of Type S-3 for our purposes is in relation to its stability; i. e., it is the least likely to change of the six reaction types described by Beck. Once the S-3 defense pattern is established, it becomes a chronic one, with few actual "shifts" in the personality components. Beck [2] refers to the chronicity of this type once it has been adopted. Molish [3] in his study of 25 state hospital schizophrenics, found that of 13 patients classed in Type S-3 as evaluated by a pretreatment Rorschach Test only 2 demonstrated a shift in type as measured by the second Rorschach. Each of the remaining 12 patients in this group, all classed in other types, showed a shift in type. In a later study of schizophrenics in a Naval hospital population, Molish [4] found the same stability for 17 patients described as S-3.

The fundamental principle of our proposed method for predicting and evaluating change is based on the courses of change for all six of the schizophrenic reaction types. However, the primary concern of this present study is in respect to Type S-3. Once the nature of any of the schizophrenic reaction types is established, it becomes possible to apply the previously described concepts of Bleuler's "extent prognosis" and "direction prognosis." The "extent prognosis" of Type S-3 is favorable insofar as the indications are that the patient will be able to maintain a very limited level of social adaptation in a self-deprived, constricted fashion if the environment is a relatively benign one. In almost all cases, there will be little or no rearrangement of the basic personality components over a period of time no matter what therapeutic interventions are tried. The process may be expected to come to a "dead end," in which the encapsulated and self-deprived level of social adaptation persists. The "direction prognosis" for type S-3 is not too favorable if we are looking for drastic changes in the personality structure of S-3 patients. However, if we consider that in this reaction type the end-state is not one characterized by severe ego disruption, the prognosis for social recovery may be considered a favorable one; i. e., in spite of their deprivation and rigidity, S-3 patients can maintain themselves in the environment.

In the present study of our representative case the first Rorschach Test, which was given prior to the insulin coma therapy, indicated that the patient was adopting the defensive pattern and over-all personality structure of Type S-3 ($r = 0.54$ with S-3; Table 4, Appendix A). At the completion of insulin coma therapy a point of diminishing returns had been reached, since the S-3 pattern was even more emphasized. It appears that had this information been utilized in an evaluation of the patient's condition at that time, subsequent therapeutic efforts would have been limited. Had the stability of S-3 pattern been recognized, therapeute efforts could have been instituted which were more modest in their goals and more considerate of the limitations

such a personality structure imposes upon the response to therapy.

However, in spite of the above, one might easily argue that there were some noted changes in the emotional state of the patient following insulin coma therapy. As already pointed out, following the insulin coma therapy there was considerably less irritability and a decline in impulsivity. Also, the self-assertive, aggressive outbursts were no longer noted. In view of these changes, one could argue that there was some improvement, since the patient's affective behavior was more manageable after the insulin coma treatment. However, the adequacy of such criteria of "improvement" must be questioned. Certainly, a decrease in irritability would make the patient's behavior on the ward more manageable, and perhaps would reduce tension within the patient herself. However, as pointed out before, the control exercised over the affect has been too exaggerated and has resulted in a reduction in emotional life to the point of over-all impoverishment. Thus, as far as ego structure is concerned, self-deprivation and constriction are the prices paid for control in the affective sphere.

The question of whether the changes noted following insulin coma therapy constituted improvement or not is not the primary concern. The important issue is the nature of the change that did occur, and it is in respect to this issue that the method of evaluating change which has been described is of significant value. By employing this method in a longitudinal study of a representative case, we not only have been able to demonstrate both the qualitative and the quantitative aspects of change but, even more important, have also provided a means of measuring this change analytically throughout all the components of personality structure. In so doing, questions regarding the more concrete aspects of describing change have been utilized: What is the nature of the change in ego functioning which has occurred? What ego losses appear or diminish in their intensity? What are the natures of the reinstituted defenses, and what are their total effects upon the personality structure?

With further research in progress, it is hoped that the longitudinal courses of other schizophrenic reaction types will be determined. Once the extent and direction of these reaction types are known, perhaps valid prediction can be made regarding their subsequent clinical courses and their characteristic responses to therapeutic procedures. For the present we have concerned ourselves primarily with the presentation of a methodology for the prediction and evaluation of change. An attempt is made to present some of the theoretical aspects underlying this methodology and to demonstrate its practicability when used for clinical or research purposes.

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Appendix A

TABLE 1.—*Personality Components and Their Levels of Manifestation*

Trait No.		Q-Sort Rating Levels of Manifestation		
		Ror. I	Ror. II	Ror. III
	I. Defenses			
	A. Constrictive			
1	Stereotyped in thought content	5	4	7
5	Breadth of interest narrowed	11	11	10
44	Fantasy blocked as defense	8	8	8
62	Blocked in thinking; in speech	11	11	10
82	Rigid hold on reality	2	3	10
85	Denial a main source of defense	6	6	6
88	Thinking inhibited, retarded (not blocked)	10	11	11
111	Suppresses Daydream activity	9	8	8
147	Attention narrowed	8	9	9
151	Affects avoided or blocked off	7	11	11
	B. Pathogenic			
56	Metaphysical or philosophical ponderings of vague, unproductive nature	4	5	4
113	Projects: ascribes his own unpalatable or painful wishes and fears to persons or objects in his world	8	7	7
114	Afraid of fantasy—fears its content	6	6	6
117	Obsessions, or phobias, of a pathological character	5	4	4
131	Overevaluation of self (compensatory for inferiority feelings)	3	5	3
	C. Adjustive			
13	Obtains frustrated gratifications in autistic fantasy roles	7	7	7
28	Suppresses emotional needs: sex, aggression, etc.	8	10	10
31	Aggressive behavior adaptive	6	6	6
51	Releases "pent-up" feelings through autistic fantasy	8	8	7
153	"Normal" phobias are easily mastered and do not interfere with mental functioning	6	6	6
	II. Associational Integration			
	A. Orderly			
11	Purposeful thinking, leading to definite conclusions	9	9	9
33	Attention adaptively adequate	7	8	8
34	Capable of making transitions from one set to another, in thinking	6	6	5
50	Language production orderly	11	12	11
79	Thinking coherent	12	12	12
102	Can think logically	12	12	12
107	Can think in both concrete and abstract terms	9	8	5
125	Has adequate reality testing	4	7	10
126	Able to concentrate	7	9	9
146	Associations (reproductive) appropriate to stimulus	7	7	7
163	Efficient in problem solving—able to synthesize	10	8	8
	B. Disrupted			
7	Dream-like thinking, with condensations and displacements in memory	2	2	2
14	Association is disrupted: perplexing and often confused statements	1	1	1
15	Spontaneity increased—undirected	1	2	2
18	Thought processes accidental—tangential	2	1	2
42	Circumstantiality in thinking	3	2	2
69	Monotopical thinking	3	3	4
74	Language production confused	1	1	1
78	Inadequate reality testing	8	5	3
89	Perseveration prevents appropriate associations	2	3	2
92	Overly concrete in thinking	5	5	9
96	Thought processes regressive	1	1	2
115	Much intrusion of irrelevant, associatively, in thinking	3	3	3
118	Confused, illogical thinking	2	1	1
123	Egocentric logic—personalized, syncretistic thinking	2	2	2
155	Regressive speech—condensations, neologisms, word salads	1	1	1
162	Prone to vague analogies and logical blunders	9	9	7
166	Attention indifferent to point of apathy	7	4	3
	III. Fantasy Activity			
	A. Autistic			
9	Autistic fantasy is strongly experienced	3	4	4
90	Unable to distinguish clearly between fantasies and reality	4	4	4
91	Life's problems solved autistically (including daydreaming)	7	8	8
116	Autistic fantasies accompanied by pleasurable affects	6	6	6
135	Affects of fantasies strongly experienced	3	3	4
	B. Regressive			
48	Primitive eroticism dominates fantasy	6	5	5
72	Affects of autistic fantasies experienced as painful	6	6	6
80	Has fantasies in which animate and inanimate are confused	5	5	3
138	Regressive themes in fantasy life	2	2	3
149	Has fantasies of bodily distortion—gross changes in body image	3	3	3
	C. Little or None			
32	Fantasy role is neither clearly self-assertive nor dependent; is static	10	10	9
43	Fantasy weakly experienced	10	10	9
76	Lacks any creative imagination	4	4	5
109	Little fantasy apparent	5	4	7
139	Permits himself little autistic pleasure	7	5	7
	D. Potentially Creative			
17	Capable of using many different themes in fantasy (in opposition to monotopical autisms)	6	7	6
19	Painful fantasy used constructively	6	6	6
25	Has imagination—in sense of vision and perspective	3	3	4
36	Fantasy activity well integrated with social and emotional life	4	4	4
47	Uses fantasies to work out real life problems	4	3	5
55	Has control of daydreams—maintains clear distinction between them and reality	7	9	8
106	Daydreams a step in actions, not end in themselves	4	6	5
119	Autisms lead to creative thinking	6	6	6
	IV. Emotional State			
	A. Lability			
22	Excessive irritability	8	4	7
26	Impulsive, unstable in reaction to usual life stimuli	11	7	7
30	Little intellectual control over basic drives	8	4	3
59	Motor loss: excessive motor alertness, i. e., purposeless, inadequate	4	3	4
70	Vacillating moods	9	3	3
97	Tantrums, and aggressive, self-assertive outbursts	10	5	9
105	Mobilized affect dominates his thinking	10	2	4
121	Control and delay—general unrest	11	7	10
129	Mood is elated or excited	9	3	4
143	Free anxiety—intense and sudden appearance, with ego control failing	6	6	6
161	Hypersensitive	7	7	9

TABLE 1.—*Personality Components and Their Levels of Manifestation*—Continued

Trait No.		Q-Sort Rating Levels of Manifestation		
		Ror. I	Ror. II	Ror. III
	IV. Emotional State—Continued			
	A. Lability—Continued			
164	Uncontrolled energy distribution	8	8	8
168	Strong affects, accompanied by anxiety	8	3	4
	B. Fixed Tone			
35	Mood painful or depressed	5	5	4
40	Affectless fantasy	10	10	9
49	Emotionally impoverished	2	9	8
81	Little externalized affective response to outer stimuli	8	11	10
103	Either gives the same level of feeling tone or is dominated by one prevailing affect	12	10	11
134	Sensitivity to outer stimuli reduced	5	10	8
140	Patient apathetic, torpid	2	9	8
	C. Controlled Release			
54	Spontaneous affect with control	2	2	2
67	Orderly changes from one emotion to another	3	6	6
71	Affects situationally appropriate	6	6	6
83	Anxieties adaptively mastered	4	4	5
86	Can be emotional without subsequent anxiety	4	5	4
122	Mood generally pleasant	7	8	7
150	Capable of showing wide variety of emotions, within normal range	4	2	2
	V. Social Adaptation			
	A. Self-absorbed			
3	Patient rejects environment	10	9	8
4	Incapable of actualizing daydream aspirations	7	6	6
12	Uncommunicative—makes little effort at verbal rapport	7	7	5
27	Patient negativistic	4	2	3
41	Interest centered on sex, bodily function, etc.	5	8	7
45	Resists all change, attempts to shape environment within his own existing system	9	5	8
52	Has little understanding of emotions of others; defect in emotional rapport	12	11	11
60	Withdrawn into fantasy, whether or not with affect and distress	5	8	5
75	Unconventional, heterodox, asocial	7	8	5
84	Disregards external stimuli	9	4	3
100	Unique attitudes and beliefs aspect of patient's adaptation	3	4	2
127	Construes "reality" in terms of his own needs	8	7	6
130	Indifferent to reality (i. e., disregards, but accurately perceives what he attends to)	10	10	5
137	Socially withdrawn: withdrawn from, or inadequate with respect to, social participation	9	12	12
156	Persistent, unresolvable conflicts in evidence	8	8	7
159	Has little understanding of emotions of others	11	11	11
160	Amoral—unmindful of social mores	4	4	5
170	Large discrepancy between fantasy roles and real-life achievement	6	6	6
	B. Self-Deprived			
8	Excessive repression (to pathological degree) of gratifying images	10	9	10
10	Unable to initiate activity	9	9	8
23	Low level of aspiration	5	9	9
24	Low productive efficiency, or anergic	9	10	11
29	Undervaluates self: inferiority feelings	6	6	6
38	Permits self little pleasure or enjoyment	10	10	11
57	Withdrawal from social contact, but not into autistic fantasy	8	7	12
58	Thinking impoverished	5	5	9
63	Excessively submissive	7	7	7
64	Has formed cramped and rigid attitudes	9	8	8
68	Inefficient use of intellectual endowment	7	8	9
93	Cautious in social contacts—afraid of doing the "wrong thing"	7	7	7
95	Passive in social adaptation—minimum of self-will	9	9	9
124	Has no pleasant pursuits	10	10	10
141	Ascetic denial of self—appears to have few needs	8	9	9
142	Achieved social level is lower than promise (in abilities)	8	9	8
148	Interests narrowed (relative to ability)	11	11	10
152	Potentialities for pleasure and learning are hindered	11	10	10
158	Motor coordination inadequate—ego function sense (slowed up or torpid)	9	10	10
165	Readily accepts inferior social roles	6	7	6
167	Overconventional	4	3	3
	C. Restitutional			
2	Fantasies of cosmic identification	5	5	5
21	Delusional thoughts—systematized	0	0	0
37	Has oral reunion fantasies	5	5	5
39	Delusional, but with some direct reference to life situation	0	0	0
66	Feelings of being "possessed" or controlled by some other person or force	3	3	2
77	Religiosity: conflict dealt with in religious terms	4	3	3
104	Experiences delusions and hallucinations of new reality	0	0	0
108	Has world reconstruction fantasies	5	6	5
120	Hallucinatory	0	0	0
132	Has fantasies of world destruction	5	5	5
133	Has "miraculous apparitions" of devil, God, etc.	3	5	3
136	Has rebirth fantasies	6	6	5
	D. Constructive Life Objectives			
6	Socially well enough adapted	7	7	7
16	Drive and energies mastered by intellectual control	3	7	7
20	Adequate motor coordination—little wasted effort	6	7	6
46	Ability for self-protection and self-care	7	7	7
53	Adaptive ability commensurate with basic intelligence	5	5	4
61	Has realistic expectations of others	6	6	6
65	Sympathetically grasps needs of others and is regardful of them	1	1	1
73	Invests himself in social institutions: home, church, clubs, etc.	2	2	1
87	Has broad interests, within adaptive social range	3	5	4
94	Organization of feelings adequate (e. g., around personal interests)	6	7	7
98	Overcomes frustrations through action	5	4	5
99	Aspiring and achieving	5	5	5
101	Capable of real pleasure and enjoyment	2	2	2
110	Capable of adjusting to usual varieties of situation	4	7	6
112	Realistic plans and goals	6	6	6
128	Can deal effectively with own life problems	7	8	7
144	Mindful of social canons, but not compulsively adherent	5	5	8
145	Forms friendships readily	1	2	1
154	Emotional warmth—able to sympathize with others	1	1	1
157	Ample energy to invest in projects and undertakings	5	4	5
169	Has adequate concept of self	6	6	6

TABLE 2.—*Outline of Treatment Program of Patient A*

Age	
14	First visit to psychiatrist
18	First psychiatric hospitalization (private hospital—2 mo., 1948), psychotherapy
19	Psychotherapy
20	Psychotherapy
21	Admitted to Spring Grove State Hospital, 1952, to present, 1957. Psychotherapy 2-3 times weekly for approximately 18 mo.
22	Rorschach Q-Sort 1 (S-3) (3/27/53)
23	Insulin and ECT (4/20/53 to 6/5/53)—48 insulin treatments (36 comas)+5 EST's Rorschach Q-Sort 2 (S-3) (6/24/53)
24	Drug therapies (June, 1954-June, 1955)
25	Placebo (June-July, 1955); reserpine (Aug., 1955, to Jan., 1956)
26	Psychosurgery (Jan., 1956); chlorpromazine (Jan., 1956 to present) Rorschach Q-Sort 3 (S-3) (4/30/56)

TABLE 3.—*Intercorrelations of Rorschach Tests I, II, and III of Patient A*

	Rorschach I	Rorschach II	Rorschach III
Rorschach I (3/27/53)	....	0.78	0.76
Rorschach II (6/24/53)	0.78	....	0.88
Rorschach III (4/30/56)	0.76	0.88	....

TABLE 4.—*Correlations of Patient A's Three Rorschach Records with Beck's Schizophrenic Reaction Types*

	Beck's Schizophrenic Reaction Types					
	S-1	S-2	S-3	SG	SR-1	SR-2
Rorschach I (3/27/53)	0.03	−0.03	0.54	0.28	0.33	0.28
Rorschach II (6/24/53)	−0.13	−0.20	0.60	0.24	0.12	0.20
Rorschach III (4/30/56)	−0.12	−0.23	0.73	0.27	0.20	0.25

TABLE 5.—*Conceptual Schema for the Six Schizophrenias (Beck)*

		S-1	S-2	S-3
I	Defenses	Pathogenic and constrictive	Pathogenic	Constrictive
II	Associational integration	Disrupted	Disrupted	Orderly
III	Fantasy activity	Little or none (if present, autistic or regressive)	Autistic, regressive	Little or none
IV	Emotional state	Labile	Labile	Labile, or fixed tone
V	Social adaptation	Self-absorbed; restitutional with some self-deprivation	Self-absorbed; restitutional with some self-deprivation	Self-deprived
		SR-1	SR-2	SG
I	Defenses	Constrictive; at times pathogenic	Pathogenic; adjustive	Constrictive, pathogenic
II	Associational integration	Disrupted	Orderly; at times disrupted	Disrupted
III	Fantasy activity	Little or none	Autistic, regressive	Little, but autistic when it occurs
IV	Emotional state	Labile	Labile	Fixed tone
V	Social adaptation	Self-absorbed; self-deprived	Self-absorbed; self-deprived	Self-absorbed; self-deprived

Appendix B

Report of a Case

Patient A was the third of four children, having two brothers older and a sister 2 years younger, who was born with a harelip. The patient was described as a very good baby, "too quiet and good." From the ages of 2½ to 4 years she had temper trantrums and was hard to deal with. She began to display a tendency to do the opposite of what was asked. In elementary school she was bossy with other children and liked children younger than herself. She chose children to associate with whom her parents did not approve of. At the age of 12 she began to show signs of withdrawing. She refused to join the Girl Scouts when invited, but did so at her mother's insistence. She would not go to dancing school as her brothers did. In the second year of high school she began to keep company with students who were not interested in their work and who cut classes. She failed. She was transferred to another high school, in which there were only girls, and she walked out of the school after one-half year, refusing to stay. She was not forced to return. About this time she began to complain of pain in her head and of stomach trouble. The patient then began to attend vocational school, which she did not like; nevertheless, she went for two and one-half years, until within six months of graduation.

The principal described her as not being able to concentrate and stated that she did not put out on a job like most of the students and that she refused to conform to standards. She got a job learning to be a telephone operator and stayed one day. Afterward she cried, saying she was too nervous. Her parents say that they "let her stay at home and help her mother." Shortly after this, the patient complained that she was losing her mind and would have to be taken to a doctor. Since the patient had been out of school, she had been going to her psychiatrist and staying at home. She did not like to be with people. She would go to movies, where she would carry on incessant conversation; otherwise she was taciturn and silent. For the past five or six years the patient had had little or nothing to say to her father. She practically never spoke to him. For the last three years

she has been absolutely mute in his presence, even though when she went to school she had to be driven there by him. Her distaste also extended to her brothers. According to the patient, her brother attempted to have sexual relations with her about the age of puberty.

The parents were described as intelligent people with a good income, who had known for many years that the patient was ill. For some reason the mother always treated the patient differently from the other children. The parents, since the patient was a small child, had had constant disagreements over her treatment. For example, the mother stated that when she punished the child, the child should not attempt to hit mother afterward. The father, on the other hand, thought that the child could hit mother back and always took her part. From childhood the child had said to her mother, "Oh, you—I don't have to listen to you." It was felt that while the parents had spent thousands of dollars on treatment for the patient, they had not given her much support or understanding. The patient's mother had been the only one she would talk to. The mother generally tried to pacify her. It was her mother who finally brought out in the open her impatience with the expense of the treatment and the patient. On one occasion, when the mother suggested the patient be quiet, the patient stayed in her room for the next two months and did not come to meals; at the end of this period she would eat only her meat, raw. The mother pointed out how she held up the other children as models for her. In the summer prior to admission the patient kicked her mother several times, called her "a legalized prostitute," and said, "I will kick your guts out." There was no explanation ever given for these statements. She continued to remain very antagonistic toward her family.

At age 14, because of increasing complaints about her stomach, she was seen by a stomach specialist, who recommended psychiatric consultation. On this occasion she was seen by Dr. G. three or four times. In retrospect, several years later, the patient remembered her visits to Dr. G. Her mother and father had not approved of him. She claimed they did not like him because he told them that he did not think anything would benefit her. The patient felt that he was right in his diagnosis. Her mother thought he did not want to be bothered with the case. The patient did not disapprove of him as much as they did. She thought he was fair. Four years later, at age 18, she saw Dr. G. again. At that time he had left it up to her as to whether she wanted to go to a mental hospital. She went to a private psychiatric hospital and was there for two months. Dr. G. saw her there two or three times a week. After her release she saw Dr. W., whom she describes as "all right and nice to her." She saw him twice a week for about two years. She feels that he kept on seeing her "because he thought she was getting something out of it." Dr. W. then referred her to Dr. C. because he was going into the service. Her father terminated her relationship with Dr. C. very shortly because he had gotten angry with the doctor because the doctor had raised the fees. The patient felt she liked Dr. W. better than Dr. C., who seemed disorganized to her.

About three months prior to her admission to the Spring Grove State Hospital, in January, 1952, she was being seen in the Phipps outpatient clinic of The Johns Hopkins Hospital. Just prior to her admission she was described as withdrawn, sullen, preoccupied, and showing no spontaneity; she felt she was going to die, said she was "scared to death all the time and can't stand it," was starving herself, slept poorly, and complained of her mind wandering. It was felt that she displayed a schizophrenic adjustment reaction and was becoming suicidal because she took an overdose of medication. At that time her status was formulated as that of a neurosis with depression and psychosomatic symptoms following sexual relations with a brother. She displayed guilt feelings and was apparently developing a schizophrenic reaction. She was antisocial, could not make friends, had feelings of reference, was paranoid and preoccupied, and had suicidal and some homicidal thoughts; commitment to a state psychiatric hospital was recommended.

Very shortly after her admission to this hospital she was presented at a staff conference. The personality and psychological studies were presented in February, 1952. Her behavior was characterized by its noticeable lack of emotion. While she would occasionally smile, grimace, or fight, one was left with the impression that it was almost a mechanical reaction. The Wechsler-Bellevue Intelligence Scale indicated a low-average range, with a fairly extensive interest variability. The impression obtained from Rorschach and Thematic Apperception Test (TAT) studies was that of a person whose attempts at relating had apparently been so frustrating that she had retreated to a ruminative and affect-isolated fantasy life. Her fantasies were basically concerned with obtaining warmth and sustenance; they were clothed in the raiment of her wish for, but fear of, mature heterosexual relations, and enabled her to achieve the happy ending in fantasy, if not in fact. She was so taken up with this fantasy that she was unable to achieve satisfaction realistically. It was the impression from this psychological study that the patient exhibited a character difficulty and that this difficulty fell somewhere in the schizoid-to-schizophrenic character category.

At this time one of the hospital physicians, Dr. R., became interested in being the patient's therapist. In retrospect, he based his selection of her for treatment on the facets of her intelligence, her age—she was only 22—some expression of dynamic content at the time (which later turned out to be superficial and mechanical expressions, which she had assimilated in her contact with psychiatrists), and what seemed like a relatively short period of illness. At first she appeared to be a good treatment case. In recalling his interest in her, he stated that she seemed to be intelligent; in the staff conference she answered questions fairly rationally and appeared to have good memory, and even her reasoning about matters not related directly to herself and her hospitalization seemed fairly good. What appeared to be a consistent trend in her productions in treatment, namely, her projection on to her parents of so much of the blame for her becoming upset at home and her eventual "unjustifiable" admission to the hospital, also seemed to have some appeal in terms of helping this girl by giving her individual psychotherapy. A few days after the staff meeting Dr. R. went directly to the patient and told her that he was personally interested in her case and wondered if she would like to spend some time talking to him about it, and also in deciding either at that time or before, if necessary, whether or not she would like to see him on a regular basis. This initial interview was held a few days later, and, although not enthusiastic—there was some aloofness and even suspiciousness—she agreed to see him on a regular basis. Dr. R.'s reaction to the interview was that she was not as responsive to the offer of psychotherapy as he had expected that she would be, and she seemed to give him the impression that if he were interested in seeing her, she would be willing to see him.

Thereafter the treatment program consisted of anywhere from two to three hours of individual psychotherapy weekly, and this continued without any significant interruption for approximately one year and a half. She was admitted on Jan. 30, 1952, and transferred to the chronic service in July, 1953, and Dr. R. saw her a few times after her transfer to the chronic service. Termination of therapy came about primarily because she refused to see Dr. R., actually refusing to come out of the dayroom and into the office. At that time she even refused to speak to him when he approached her in the hall or went to her room. This rejection of the therapist, her withdrawal from him and hostility toward him, was a consistent feature of therapy, especially after approximately the first three months, and there had been times when she had refused to come to the office for a therapy hour, even during the first six months. Her final refusal to see Dr. R. after her transfer to the chronic service was interpreted as being a result of her loss of faith in him, that is, whatever faith she might have had, plus the fact that, unfortunately, he had been at times in an administrative relation to her and had on numerous occasions to refuse her demands that he simply let her go home, or that he give her ground privileges which she had abused. Another reason, he felt, for her gradual, and then abrupt, withdrawal from therapy was the coincidence with what appeared to be a definite deterioration, in comprehension, memory, and rational thinking, but also with the appearance of rather definite paranoid ideation. Actually, there was a strong paranoid coloring from the very beginning, but her reasoning was still reality-bound, and it was this specific feature which seemed to drop out of sight, so that her paranoid ideas became paranoid delusions. He had never witnessed, nor had he seen any indication of, hallucinatory experiences. In the interview situations, especially after the first five or six, she became more and more hostile toward the therapist. From the very beginning she expressed considerable hostility toward her father and mother, as well as one of her brothers. One of the commitment papers suggested that this particular brother had had intercourse with the patient some time prior to her admission to the hospital. When asked about her previous therapists, she spoke of them quite superficially and impersonally, so that Dr. R. often wondered to what extent there had been actual individual psychotherapy in the past. One of her chief concerns about herself was her acne, and she frequently blamed the therapist for not being able to prescribe medicine and treatment which would help this condition.

As time went on, the vituperative hostility which she early expressed toward her parents began to be directed toward the hospital, particularly certain personnel on the ward, and also the doctors, including the therapist. Eventually the therapist was the prime instigator and cause of her unhappiness in the hospital, and she related this consciously to the fact that, although he had it within his power simply to discharge her, he did not. She seemed to have a sense of humor which at times could be elicited, and another doctor, Dr. H., seemed particularly able to reach her in this manner, through a kidding technique, but this never carried over into Dr. R.'s therapy with her. When she was particularly accusing toward, and disparaging of, the therapist, he attempted to point out, on the basis of logic and rational thinking, the inconsistencies and the distortions which characterized her verbal attacks. At times it was felt necessary to become quite direct, and at times the therapist showed open irritation and anger. The basis for the therapist's showing anger seemed to be the necessity to effect some control and give some structure to the therapeutic atmosphere, which

otherwise would have deteriorated completely because of the patient's unbridled and unreasonable verbal attack.

About two years later, when the patient was interviewed as to her feelings about Dr. R., she stated at first that she did not know; then after a pause she said she felt he was unfair in some respects. "He blamed me for being out of bounds one time and cancelled my ground parole and then transferred me from C ward to A ward, which turned out to be a trap to give me insulin. I didn't think of that until later." The thing that impressed this interviewer was the complete lack of any positive feeling that she seemed to display for this relationship and the complete lack of any insight into or understanding of what was being attempted in all of the psychotherapy that she had received.

On the ward during the time she was receiving psychotherapy with Dr. R., she was observed to disturb other patients with her hostile staring and glances, but rarely entering into anything other than verbal encounters. Every situation was turned into a state of affairs where she felt she was being abused and a constant complaint of her being in the hospital. She was constantly challenging her therapist to tell her what was wrong with her and saying that he was mixed up with some scheme to keep her in the hospital. She avoided her ward physician completely but complained about him to her therapist. She continued to beg to go home, although blasting her parents for rejecting her. She seemed able to express herself quite clearly. She displayed swings in her behavior from an extreme, characterized by speaking in very low tones, as little as possible, and to as few people as she could. At other times she became very demanding. She, at times, attempted to elope, and whenever she was given ground parole she inevitably managed to stir up anxiety because of her threats to run off. She appeared to develop no positive attachment to anyone in the hospital. As the result of this increasing regression with the intensifying paranoid expression, it was decided to try this patient on a course of insulin coma therapy. It was at this time that the patient was administered Rorschach Test I (March 27, 1953), since she was one of a group of patients in whom the effects of insulin coma therapy were being studied.

The patient began deep insulin therapy on March 30. She ran a rather cyclical course in that at times she was friendly and at other times she displayed her usual sulky, antagonistic behavior. No particular changes were noted. Following insulin therapy several attempts were made to have her participate in vocational rehabilitation, but she remained uncooperative and on several occassions tried to elope. It was also observed that visits from her family disturbed her.

In June, 1954, the patient was placed on treatment with chlorpromazine. The dose that she was receiving varied from 200 to 400 mg. per day, and no particular effect was noted. This first course of treatment lasted eight weeks. She was started on a second course of chlorpromazine (Thorazine), receiving 100 mg. t. i. d., and was on this drug for five months, with no particular changes in her behavior or attitudes. In August, 1955, she was transferred to another service in the hospital. She resented this very much. She was then placed on placebo medication, with no apparent effect. This was followed by a course of reserpine, in a daily dose of 2 to 4 mg. with no particular results. It was finally decided, because of the patient's extremely poor progress and lack of results with her previous treatments, that a lobotomy might at least help her make a more comfortable adjustment to the hospital environment, where she continued to express a great deal of sullenness but with no overt acting out of any hostility.

A prefrontal lobotomy was performed January, 1956, and shortly thereafter she became agitated, disturbed, and hostile, and all her symptoms seemed exaggerated. She was then placed on 50 mg. of chlorpromazine t. i. d., and she became less disturbed. She has continued on this medication to the present time.

In recent months there has been some improvement, indicated by the fact that it is easier to get her to participate and cooperate in ward routines: She will allow herself to spend some time in the patient typing pool, where she is always conspicuous by the almost grotesque manner of wearing her facial make-up. During this time, on a trial weekend visit to her home, she ran away and visited Dr. G. She later stated she ran away from home because she felt that "she was not welcome." She had gone to see Dr. G. because "he had never thought of giving [her] insulin or a lobotomy."

In her periodic interviews with the present observer (A. A. K.) the patient has continued to display the same blocked, inhibited, withdrawn attitude, with no capacity to elaborate on or discuss any of the brief comments she might present during an interview, which has a minimum of any interaction and has to proceed on a laborious question-and-answer method, with frequent periods of silence.

At the present time she is not considered even a good candidate for boarding care. On the ward she tends to live in an isolative manner, with little relation to the other patients.

In presenting this case there are factors which stand out in retrospect. The first psychiatrist who saw the patient at age 14 expressed an opinion, based on his clinical evaluation, that the patient did not have a good prognosis. The family, especially the father, resented this and for years insisted on all types of treatment, and when the

patient finally entered this hospital, several years ago, in spite of unrewarding treatment responses, pressured the hospital administration for each treatment which was available until the whole gamut had been gone through.

The course of events was always one in which the hospital administration had found itself repeatedly in the position of stating, "We don't think she is a good candidate for this particular type of treatment." Yet each program of treatment was finally undertaken on the basis of its not being able to say with 100% finality that she would not respond or that there were any tests available which could have backed up a hospital administration in not undertaking all of these therapeutic ventures. Exposure to psychotherapy by psychoanalytically oriented psychiatrists over a period of several years, both prior to and following her admission to the hospital, was completely unproductive of any change. Perhaps the technique described in this paper might find its greatest usefulness at this point in helping to make a definite decision relating to other therapies.

Dr. Isadore Tuerck, superintendent, Spring Grove State Hospital, gave helpful encouragement with this project, and the Friends of Psychiatric Research, Inc., gave financial assistance.

Objectivity of the Sedation Threshold

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Introduction and Problem

During the last few years a number of papers have appeared in the medical journals which have been concerned with the "sedation threshold."[1-4] Briefly, amobarbital (Amytal) sodium is injected intravenously at a specified rate until certain EEG changes occur in association with the onset of slurred speech. The concept of the sedation threshold owes its inception to Shagass, who defines it as "the amount of sodium amytal, in mg/kg, required to produce an inflexion point in the 15 to 30 c/sec amplitude curve, which occurs within 80 sec (1 mg/kg) of the time when slur is noted."[4] Shagass goes on to say that "the slur localises the threshold roughly, the EEG inflexion point does it more precisely."

During the course of a preliminary investigation into the general usefulness of a patient's sedation threshold as measured by the onset of slurred speech, we were impressed by the apparent lack of objectivity of the onset of slurred speech, and by the disturbing possibility of its being affected by the clinical picture presented by the patient during the course of the amobarbital injections. As a result of this, an attempt was made to assess the amount of agreement among observers with regard to the onset of slurred speech following the injection of amobarbital sodium. The present paper is a report of this assessment.

Method

Seven consecutively admitted male patients were given intravenous amobarbital in accordance with the instructions given by Shagass[4]; i. e., amobarbital sodium was injected intravenously at the rate of 1 cc. every 40 seconds, each cubic centimeter containing 0.5 mg. of amobarbital sodium per kilogram of body weight. Twenty-five seconds after each injection the patient was asked to repeat the following words: siesta, saucer, sociology, solicitor, Somerset House, British Constitution, and Massachusetts. Injections were continued until the patient was no longer able to repeat the words, or until the amobarbital sodium solution was all given.

The whole procedure was recorded by means of a Grundig Stenorette tape recorder. Precautions were taken to minimize the amount of information disclosed about the patients in the recordings.

The seven recordings were subsequently played during a medical staff meeting, when 16 members were present. Members were asked to note the point in each record at which slurred speech definitely occurred. Care was taken that members gave their own opinions and were not influenced by those of others present.

Results

The distributions of opinions regarding the onset of slurred speech for the seven patients are given in the accompanying Table. Thus, for Patient 1, one of the staff thought slurred speech was apparent after 3 cc.; three, after 4 cc.; one, after 5 cc., and so on.

Distribution of Opinions as to Onset of Slurred Speech in Seven Patients

Patient No.													
1		2		3		4		5		6		7	
Cc.		Cc.		Cc.		Cc.		Cc.		Cc.		Cc.	
1		1		1	2	1		1		1		1	
2		2		2	6	2		2	1	2		2	
3	1	3		3	2	3		3	0	3		3	
4	3	4		4	2	4	1	4	0	4		4	1
5	1	5		5	3	5	2	5	1	5		5	0
6	0	6	3	6	1	6	2	6	6	6		6	0
7	0	7	4	7		7	3	7	3	7	2	7	0
8	2	8	1	8		8	6	8	2	8	6	8	1
9	1	9	1	9		9	1	9	1	9	1	9	0
10	1	10	0	10		10	0	10	1	10	1	10	0
11	2	11	3	11		11	1	11	1	11	2	11	6
12	1	12	4	12		12		12		12	1	12	5
13	2	13		13		13		13		13	0	13	2
14	0	14		14		14		14		14	1	14	0
15	1	15		15		15		15		15	2	15	1
	15*		16		16		16		16		16		16

* One member failed to record.

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It will be seen from this Table that the amount of agreement among the observers is appreciably less than might have been expected. Even for Patient 3, who was asleep after 6 cc., opinions as to the end-point ranged from 1 to 6 cc.; i. e., every possible end-point was mentioned.

Comment

First, it would appear that the onset of slurred speech depends almost as much upon the observer as on the patient. In this connection, the forms of the distributions of the opinions given in the Table are important. If the range of opinions were due primarily to errors of judgment, some sort of Gaussian distributions could be expected. The distributions are, however, rarely Gaussian, and some (e. g., those for Patient 2) are frankly bimodal. These distributions suggest that the onset of slurred speech is a subjective rather than an objective occurrence. One of the many difficulties encountered was the occurrence in some patients of a dry mouth, which tended to disrupt their articulation. This, in some cases, improved as the injection was continued.

It would appear from these findings that the onset of slurred speech cannot be used as an accurate indicator of the sedation threshold. What is more important is that this finding throws considerable doubt on the objectivity of the sedation threshold proper. It will be remembered that the sedation threshold is defined as "the amount of sodium amytal, in mg/kg, required to produce an inflexion point in the 15 to 30 c/sec amplitude curve, which occurs within 80 sec (1 mg/kg) of the time when slur is noted," and if a discrepancy of more than 80 seconds obtains between the EEG inflection point and the onset of slurred speech the threshold is considered to be invalid.[4] But, as we have seen, the onset of slurred speech is subjective and depends to a large extent on the observer. The sedation threshold cannot, therefore, be any more objective than the lack of objectivity of slurred speech will allow.

Finally, we have noticed in our work how extremely difficult it is not to be influenced by the clinical picture presented by the patient when the onset of slurred speech is being determined. Even when the patient is "removed," as it were, by listening only to the repetitions of the words in the recordings, one of our consultants was able to diagnose correctly six out of the seven patients in the experiment, even before the first cubic centimeter had been injected!

On the positive side, it is undoubtedly true that some of the patients can tolerate more sedation than others. For example, one of our patients was asleep after 6 cc. of amobarbital, while another was still awake after 15 cc. This finding alone would suggest that a refinement of the present concept of the sedation threshold, so as to make its measurement more objective, may be well worth while.

Summary

An attempt is made to determine the sedation threshold of seven male patients, employing the technique described by Shagass and using the criterion of the onset of slurred speech.

To make the procedure as objective as possible, the results are tape-recorded, but 16 listeners were unable to agree regarding the onset of speech slurring. The conclusions are that speech slurring is too subjective to be of general use and that some doubt is thrown on the objectivity of the sedation threshold.

[EDITORS NOTE: After correspondence with the authors and Dr. Shagass it has been agreed that the conclusions of this report refer explicitly to the phenomenon of speech slurring and not to the "sedation threshold" as determined by the EEG inflexion point.]

Our colleagues helped in assessing the recordings, and Dr. Charlton, physician-superintendent of the hospital, permitted us to publish the data.

Banstead Hospital.

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Simultaneous Occurrence of Psychotic Episodes in Monozygotic Twins

Psychodynamic Evaluation

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This paper is a report of the simultaneous occurrence of psychotic episodes in a pair of 21-year-old monozygotic twin girls, with discussion of the psychodynamic factors involved. The occurrence of psychosis in twins is a striking phenomenon, the etiology of which has been debated by various schools of thought. Most authorities agree that the etiology involves genetic, dynamic, psychological, and cultural factors. Gedda [1] made an extensive survey on the subject of twins and reviewed the world literature prior to 1949. Gordon [2] described twins as being more closely related to each other than to their other siblings, with an undoubtedly greater physical and emotional affinity between them. The occurrence of psychosis in twins was formerly described as a special type of psychosis by some German authors under the term *Zwillingirresein*, and by some French authors as *folie gémellaire*. They emphasized the genetic factor in describing the simultaneous appearance of psychosis in twins living apart, thereby eliminating the possibility of induced mental manifestation. Slater and Shields [3] combined an analysis of procedural technicalities in the use of the twin-study method with a presentation of 297 psychotic sets, emphasizing the genetic theories of the given disorders. Similarly, Kallmann [4] stressed the importance of blood relationship and the inheritance of factors which predispose to psychosis. He [5] also demonstrated that the correlation of neurotic and psychopathic behavior is much higher in monozygotic than in dizygotic twins.

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Psychodynamic studies of twins have only recently been described. Okada [6] followed the personality development of nine pairs of monozygotic twins over a 10-year period. He noted considerable variation in personality trends within each pair, depending on relationship with parents and other dynamic factors. Burlingham [7] studied three pairs of identical twins and described their emotional, instinctual, and interpersonal reactions, as observed in a residential nursery under wartime conditions. She pointed out that it was difficult to determine how much of their similarity was due to their basic biological identity and how much to their identification with each other. Intense rivalry was observed, and later this rivalry may be compensated for by an active resolve to remain as close to the twin as possible. Karpman [8] reported the analysis of one of a pair of fraternal twins. Acute competition between the twins was also observed but was expressed in many forms that were unrecognizable.

Report of a Case

Background and History

The twins were second-generation Americans of Irish descent. Their father, aged 50 at the time of the twins' admissions, was a ship fitter. He used liquor occasionally to excess, but this did not become a family problem. He has been described as generally quiet, reserved, and easygoing. The twins were fond of him, and he was always impartial in showing his affection for them.

The mother, of the same age as the father, lost both parents in childhood and was brought up by an aunt. She described her childhood as "lonely and unhappy." She worked as a telephone operator until her marriage. For years she had had heart trouble and hypertension. Throughout the entire

pregnancy with the twins she was sick, and at the time of delivery she was preeclamptic. The mother seemed to be the dominant figure in the family and was always concerned about her children's welfare.

There were six siblings, the twins being third in order of birth. The eldest, a boy, was reported to have experienced a "nervous breakdown" while in the Navy and to have responded to several electric shock treatments. No further details were available. The siblings appeared to have maintained good relationships with the twins with the exception of an older sister, who reacted toward them with a domineering and resentful attitude.

The twins were born in a local hospital on July 15, 1932. The birth was a difficult one. The attending obstetrician reported that the twins were born with one placenta, two cords, and two membranous sacs.

Helen was born first, weighing 6 lb. 4 oz. (2835 gm.). Betty was born one and a half hours later, weighing 4 lb. (1814 gm.). Helen was always the stronger and healthier of the two. Betty remained underweight and anemic for many years, her appetite being always poor. Both started walking and talking at about the age of 2 years. Enuresis stopped at the age of 3 years. Both started school at 6 years and continued through high school. They were considered good students. The twins were close to each other throughout their school years. They slept in each other's arms. They went everywhere together and took part in all school and social activities together.

Helen developed a ruptured appendix at the age of 7 years, which required an emergency operation. She was also involved in an automobile accident at 11 years of age, in which she received a cerebral concussion. In each of these incidents the mother focused considerable attention upon her. Betty sprained her ankle at 11 years. This necessitated several days at home. About once a year after that she sprained one or the other of her ankles. Each injury required several weeks of home care. On one of these occasions, while Betty was being carried to the table by her father, Helen called her a "faker" and said there was nothing wrong with her and that she was simply looking for attention.

Both girls recalled certain teachers with fondness; they stated that they liked these teachers because they felt relaxed and less restricted with them. They also pointed out that these teachers were different from their mother in that the latter was "always directing" and saying "don't do this and don't do that."

At 16 Betty started having dates with boy friends. Helen followed likewise several months later. Betty often mentioned that she had boy friends first and that she was more popular with the boys. Her choice in boy friends was often indiscriminate. There was frequent friction between Betty and her mother because of this. Her friends included, among others, boys of rather poor reputation and, in recent years, married men. Betty could not see why her mother objected to these fellows. Although Helen was more attractive, Betty was more successful in attracting boys and had more dates. Betty had a tendency to be sly and cunning and maneuvered indirectly to gain the desired end.

One night, at the age of 19, while waiting for a late bus to go home after work, Helen met the husband of a very close friend. He suggested that they take a short walk while waiting, and she agreed. When they reached a secluded schoolyard, he suddenly pushed her behind the schoolhouse and attacked her sexually. She fought vigorously and, during the struggle, lapsed into semiconsciousness. Her assailant became frightened, put her into a taxi, and sent her home. She recovered consciousness after she reached home. The family doctor was summoned and found her in a state of shock. A gynecological examination confirmed her statement that she had been raped. Her assailant was apprehended, tried, and sentenced to state prison.

Helen reacted to this traumatic incident with considerable fear and anxiety. She became apprehensive and did not want to see anyone, especially men. She would not let her father or brothers into her room and displayed great fear of them. During the trial she became greatly interested in the legal procedure and later expressed the hope of studying law to become a prosecuting attorney and "putting men like that away for life." The desire to study law persisted, and she had numerous arguments with her mother concerning it.

After the rape incident, Helen received considerable attention from everyone, especially her mother. Betty seemed to feel neglected and began to complain of numerous aches and pains. She complained especially of pain in her legs and feet, but repeated x-rays were consistently negative. These complaints gradually subsided.

In September, 1952, about one year after the rape incident, it became obvious to the mother that both girls had undergone a definite personality change. It had been coming on gradually. Helen became more talkative, aggressive, critical, argumentative, and unmanageable. She talked in a loud, high-pitched voice. She sang a lot, loud and off key. In addition to her determination to go to law school, she indicated her intention to become a night-club entertainer, a singer, a model, and a painter. Helen had previously shown talent in painting class in high school.

In September, 1952, Helen had what appeared to be a "fainting spell" while at work at the tele-

phone exchange. She was taken home, returned to work after a week, and had another "fainting spell" about two weeks later. During the next several months she had similar "spells," which always occurred when she was among many people and which resulted in considerable attention for herself. Her mother became quite concerned about her and suffered an aggravation of her own cardiac condition.

At about this time Betty began buying clothes, dishes, and various other items on credit. She seemed to be buying just for the sake of buying. She wanted to include a car and a piano among her new possessions, but was discouraged from doing so. Betty became very flirtatious, cultivated the acquaintance of many service men, and appeared to have become preoccupied with male friends in general. She showed increasing lack of judgment in her choice of friends and in her deportment.

In January, 1953, Helen asked her employer for vacation time. He told her that her vacation time was not due for a month or so and that he could not make an exception in her case. Helen became angry and resigned her position on the spot. She then began a series of successive adventures, in complete disregard of parental admonition and opposition. These events included enrolling in a model-training course and being rejected; taking part in a hundred-hour marathon in the March of Dimes campaign, and then moving to Boston, despite parental protest, and establishing residence in a hotel. She preferred to walk 4 miles to her favorite restaurant for meals, and there led a convivial life, with casual acquaintances. Among these was a self-acknowledged free-lance photographer, who induced her to pose at his "studio" for commercial posters. Another fellow promised to book her as a singer and entertainer at some night clubs and theaters. None of these prospects materialized, and she was also unsuccessful in finding work as a switchboard operator.

Two episodes with would-be marriage partners occurred—one partner a self-styled talent scout, and the other a delicatessen cook, representing himself as a millionaire. After leaving home twice without permission and without adequate funds, Helen was brought home by the police, on March 6. Her parents then arranged to have Helen taken directly to the state hospital.

On Jan. 30, 1953, about two weeks after Helen left for Boston, Betty suddenly decided to take a trip to Florida. When she announced the news to her parents, they were incredulous and objected, but she continued her preparations for the trip. On Feb. 1 she left by plane for Florida. Betty later claimed she went there primarily to locate a soldier boy friend who was then stationed at an Air Force Base in Florida. She said she was not really serious about him but looked upon him simply as another boy friend. After missing the midnight bus to the Air Force Base in Valparaiso, she decided to stay awake and take the next one. Not the least sleepy or tired, she arrived at the Air Force Base at 8:30 a.m. and immediately went to the personnel office looking for her soldier boy friend. She finally located him, and they had breakfast together. She suggested a date for the evening, but he claimed he already had a date with another girl.

She then embarked upon a spree of irresponsible behavior similar to her sister's. She sang and danced and was up all night with casual acquaintances, including soldiers and men she met in this vicinity. On Feb. 6 she met three men at a local tavern in Valparaiso who invited her for a ride, and she accepted. They drove across the state line to a town in Alabama, where she claims they attacked her sexually. Then they drove her back.

On return to her hotel, she reported the incident to the sheriff and preferred charges against the men. The sheriff put her in jail on Feb. 8 where she claimed that she was held as a material witness. The men were never located. On Feb. 17 her mother heard about this difficulty and wrote her an urgent letter, begging her to come home immediately. Betty refused and preferred to wait until the sheriff officially informed her mother that she was raped, as she was afraid her mother would not take her word for it.

After considerable "to-do," Betty was sent back home on March 5 by plane, under supervision of the Travelers Aid Society. She did not want to come back and tried to get away from the plane on one of its stops. While on the plane, she was euphoric. She sang and talked to many of the passengers, and she tried to get their autographs. After she arrived home, she continued in this overactive mood and disappeared from home twice during the next several days. Her parents then had her brought to the hospital, on March 9.

Physical Examination.—Both twins were well developed, well nourished, attractive girls of 21, in good physical condition. There was a strong facial resemblance, and both twins had brown, wavy hair and blue eyes. Physical characteristics were as follows:

	Helen	Betty
Height	5′ 3″	5′ 2″
Weight	106 lb.	98 lb.
Blood pressure	138/80	128/70

Betty showed a slight degree of atrophy of muscles of the left thigh and leg, with no impediment in walking or running.

Cardiovascular Systems: Normal in both twins.

Neurological Examination: Essentially negative in both twins except as mentioned above.

Dental Examination: Each patient had a partial denture, replacing the two upper central incisors and the two adjoining lateral teeth, and both had occlusal fillings in No. 12 and No. 13.

Blood Typing: Both had O, Rh-positive grouping.

Anti-	A	B	C	D	E	e	M	N	S	P	K	Le^a	Le^b	Fy^a	C^w
Helen	0	0	+	+	0	+	+	0	+	+	0	+	0	0	0
Betty	0	0	+	+	0	+	+	0	+	+	0	+	0	0	0

Fingerprint Readings: The readings were consistent with a diagnosis of monozygotic twins.

Electroencephalogram Report: The over-all impression was that the two EEG's were very similar.

Genetic Report: These girls meet the criteria of monozygotic twins as described by Kallmann.[8]

Psychometric Report: Both girls were administered the Wechsler-Bellevue Intelligence Scale, Form II. The results were as follows:

	Helen	Betty
Verbal-Scale I. Q.	109	100
Performance-Scale I. Q.	113	96
Full-Scale I. Q.	111	98

Mental Status.—The sensorium was clear in both girls. They were correctly oriented in all spheres, and memory was unusually acute for both remote and recent past. Both patients were very alert mentally and quick to detect any minor error or inconsistency in conversation. However, insight was absent and judgment impaired.

Both twins were quite cheerful and rather elated, although both manifested irritability. The girls were overtalkative and spoke rapidly, with a rapid association of ideas, to the extent of becoming almost incoherent at times. They easily became involved in details and elaborated on trivial and irrelevant items. Both twins were also rather expansive and had ambitious plans for the future, since they both considered themselves quite talented.

Helen had a tendency to argue and "split hairs." She was aggressive, impatient, and critical and would force others into a defensive position. Betty was more cautious and was careful not to start an argument that she could not win. While Helen was determined to carry out her wishes by bringing pressure to bear by one means or another on the persons involved, Betty showed no overt aggressiveness and appeared more compliant. Betty was just as determined to have her own way but was shier and more cunning, using the indirect approach, rather than the "frontal attack," as used by Helen.

After admission, Helen's hostility toward her mother flared into the open. She blamed her mother for her hospitalization and said that her mother should be ashamed of herself for having done this. Helen also accused her mother of having been suppressive and directive since childhood. She still planned on becoming a night-club entertainer and claimed that her mother had old-fashioned ideas about the entertainment world. She remained very sarcastic toward her mother and could not seem to hurt her enough with cutting remarks and hostile notes. Meanwhile, she expressed love and admiration for her father and was sure he would "understand." Helen often dwelt on the rape incident during conversation. She would go into great detail, relating how her assailant pounded her head until she became unconscious. She gave equally detailed accounts of the trial and still hoped to become a lawyer. She claimed that the trial had stimulated this interest.

Betty, in her conversation, reflected Helen's desire to become an entertainer. Betty described how she had sung for the servicemen and acted as hostess. She often talked about her trip to Florida and how much she had enjoyed herself there. She tried to continue her romantic attachments by writing frequent notes to several of her acquaintances there and reminding them of the good times they had had. She was so happy with her memories of Florida that she planned on going back there in the near future, despite the supposed trauma she had experienced there. She ruefully observed that her mother did not seem to take her "rape incident seriously" and stated that her mother did not believe she had been attacked. She felt that Helen somehow seemed to get all her mother's attention.

Hospital Diagnosis: Manic-depressive reaction, manic type.

Clinical Course.—Both girls were allowed to remain together for observation on the receiving ward, and their behavior during the first two weeks proved to be disturbing to the others, chiefly because they both sang continually. This annoyance ceased as the newness wore off, and the differences in their behavior patterns became apparent.

Helen was quite vindictive toward Betty and ridiculed her mercilessly in the presence of others. When both were placed in the same group for therapy, Helen made Betty so uncomfortable that it became necessary to place them in separate groups. Betty also complained that her mother was paying far more attention to Helen and that she was practically ignoring Betty. It was noted by ward personnel that there was some truth in Betty's observation. Betty then became more energetic in bidding for her mother's attention. She solicited kisses from her mother at visiting time, and did her best to out-talk Helen during the visit. Another technique she employed was to attempt to incorporate a fellow patient into the visiting session. On several occasions, just as her mother was about to leave, Betty threw herself on the floor in an apparent faint, similar to those which Helen had experienced.

Another development was Betty's attachment for her group leader in psychotherapy. She began

calling her "Mommy" because, as she put it, "She understands me and is nice to me." She expressed a desire to enter training and become a nurse, like her group leader. She constructed a nurse's cap and frequently wore it around the ward. Betty also became involved in a homosexual relationship with another patient, which lasted about two months. She had kissed her several times, wrote notes to her, and sent her gifts. She had never previously demonstrated tendencies of this type; nor did she subsequently.

By the end of August Helen began to show improvement. Her bold and aggressive attitude began to disappear. She was not as critical as formerly, and she became more compliant and friendly in her attitude. She herself observed that she did not feel like arguing with everybody, as she formerly did. Betty's improvement lagged behind Helen's somewhat, beginning in September, but by October the improvement was obvious. She was not as overtalkative, overactive, or excitable as formerly, and her judgment also improved.

The twins continued to show further improvement during November. In December, they were allowed home for a 15-day period over the Christmas holiday, during which they went visiting and shopping together. They preferred to be in each other's company most of the time, and when their mother offered them separate rooms during the visit, they insisted on sharing the same room and the same bed. Betty was a little more active in her desire for them to be together than Helen was. Both girls had become very quiet, pleasant, and congenial. Several neighbors called the mother by phone and told her how pleased they were to see the girls back and "their old selves again." After a brief check-up following their return from visiting home, the medical staff felt the twins had recovered from their psychotic episodes. They were released from the hospital on Jan. 16, 1954, in their mother's care. They have since made a satisfactory adjustment at home and have become gainfully employed. No organic therapy was administered during their illness.

Psychodynamic Evaluation

The rivalry between the two girls for their mother's attention and affection had been intense since early childhood. Both girls resorted to devious and involved maneuvers to gain their ends.

Helen, who was the first-born, was the more dominant, responsible, and competent of the two. Betty often looked to her for moral support. Helen was always available to help her mother in household chores and in many "little things." She often presented her mother with gifts. The mother was unaware that Helen had been her favorite all along. For example, in showing pictures of the twins as children, the mother took from her bag an individual picture of Helen and then took out a family group picture in which Betty was one of the group.

Betty keenly resented Helen's success in attracting the mother's attention and affection. She remarked, "Although I was the anemic and sickly one, Helen always seemed to be getting all the attention."

In her search for affection and security, Betty turned her attention to members of the opposite sex. She began to show active interest in boys at about 14. Her mother did not allow her to go out on dates until she was 16. Once started, she became more active and successful than Helen in her relationship with boys. Helen became envious of Betty's success in this direction. During her psychosis this envy turned to open hostility, and Helen became vindictive and very abusive toward Betty.

Another point of interest is the chain of events following Helen's rape incident. During Helen's convalescence from the attack, her mother lavished almost all her attention and affection on Helen and practically ignored Betty. Betty found herself in a complex emotional situation. Because she identified herself so closely with Helen, she felt very bad about Helen's plight. But, what was even more important, Betty lost what little attention her mother had given her before. She felt herself almost completely ignored and practically rejected by her mother. In a desperate attempt to recapture her mother's attention, she was driven to patterning herself after Helen to the extent of being "raped" in Florida, as Helen had been.

At the height of the psychotic episode, Helen's attitude toward her mother changed radically from love to intense hatred. Her love and admiration for her father at this time became paramount. In addition to resenting her mother's alleged directive and repressive attitude, she showed rivalry with

her mother for her father's affection. She claimed her mother was jealous because she herself could cook better. Helen also claimed that she enjoyed the same things her father did, i. e., sports, popular music and dancing, etc. She recalled that her mother objected to popular music and dancing, whereas her father often danced with the twins. She said of her father, "He is the nicest father in the world, very nice looking." She claimed her father did not want her hospitalized, but that it was her mother's idea.

Betty also spoke of her father with warmth and affection but did not show the strong rivalry with her mother that Helen did. Although Helen tried to monopolize her father's attention and affection, he shared his attention equally with the twins.

In Betty's homosexual experience mentioned above, she apparently identified the other patient with her twin sister, for whose affection she yearned. To carry this point further, a narcissistic attempt to establish identity should also be considered.

To sum up this discussion, it appears that the following psychological factors contributed to Helen's breakdown:

1. Intense rivalry with her twin especially for (*a*) her mother's attention and affection and (*b*) popularity with members of the opposite sex.
2. Rivalry with her mother for her father's affection.
3. Traumatic experience of rape incident.

Those factors leading to Betty's breakdown were as follows:

1. Intense rivalry with twin for mother's affection and attention.
2. Feeling of anxiety and insecurity as she felt herself loosing struggle in the rivalry with her twin.
3. Seeking love and security from her twin even through homosexual attachment, i.e., substituting homosexual partner for twin.

The simultaneous occurrence of a similar type of psychosis in twins or in two or more people living in close association has often been referred to as folie à deux. Many other terms have been used to describe this phenomenon, e. g., associated insanity, psychosis of association, influenced psychosis, induced psychosis, simultaneous psychosis, imposed psychosis, etc. These terms are often considered as subdivisions of folie à deux.

The term folie à deux is usually reserved for a specific type of occurrence. It refers to the appearance of a similar type of psychosis in two or more people living in close association. These may be twins, siblings, parent and child, husband and wife, etc. The dominant partner, or one with the stronger personality, develops a psychosis first. This is usually a paranoid type of psychosis, characterized by persecutory delusions. The weaker, or more submissive, partner soon acquires the same psychosis, delusions and all.

Gralnick[9] reviewed 103 cases of folie à deux and the entire English literature prior to 1942. He emphasized the psychodynamic factors in transmitting a psychosis from one person to another. He found that it occurs more frequently in females than in males, in a ratio of 4:1. It is especially prominent in sister combinations and next commonest in mother-and-daughter pairs. He discounts "constitutional predisposition" but emphasizes instead "cultural factors." He observes that women's role is mostly restrictive and submissive. This passive psychology, he states, renders them more suggestible and ready to identify themselves with, and depend on, a stronger person, such as a mother or mother-substitute (sister).

Oatman[10] states that in a large majority of cases of folie à deux, the syndrome presents itself as a paranoid psychosis, with both patients entertaining almost identical systematized, plausible delusions, but not the bizarre, primitive beliefs of schizophrenia. He claims the remaining cases are usually classified as manic-depressive. He further states that an adequate history will reveal that one member of the pair exhibited psychotic symptoms earlier, if only by a matter of days.

Although the case presented in this paper does not meet the classic description of folie à deux in that the paranoid features of the psychosis are not present, there are several

features suggestive of this syndrome. They are as follows: (1) Helen, the first-born, was more dominant and aggressive, and (2) Betty's case was one step behind and paralleled Helen's case to a large extent.

Summary

The simultaneous occurrence of psychotic episodes in a pair of female monozygotic twins is presented. Some of the dynamic factors involved are discussed. Resemblance of this case to the folie à deux syndrome is also considered.

16 Chapel St.

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Pyrocatechol Amine (Catecholamine) Metabolism and Effects of Electroconvulsive Therapy

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A number of theories purport to refer the etiology of psychoses to a disturbance in the metabolism of the sympathetic neurohumors[1,2] or to an alteration in the functional activity of the sympathoadrenal system.[3,4] Similarly, some of the explanations advanced to clarify the role of electroconvulsive therapy (ECT) utilize the same frame of reference.[5] Such hypotheses ought to be verifiable directly by the investigation of the metabolism of pyrocatechol amines (catechol amines) in psychiatric patients.

The release of pyrocatechol amines at sympathetic postganglionic nerve endings and from the adrenal medulla is well known,[6] of course; but very little is understood about this release as it occurs after electrically induced convulsions. The finding by Weil-Malherbe[5] of an elevated plasma epinephrine following ECT has provided more direct evidence of sympathetic involvement than had previously been available in man. Pekkarinen et al.[7] have reported that administration of electroshock to rabbits on 10 successive days resulted in an increased adrenal size without change in the absolute amounts of pyrocatechol amines in the glands. More recently it has been found in this laboratory that a single electroshock given to rats is followed by a rapid loss of amines from the gland, with a subsequent repletion period lasting eight to nine hours.[8] No significant change in adrenal weight was observed. The present paper approaches the problem from yet another direction, namely, the relation between the rate of excretion of pyrocatechol amines in the urine and the clinical result of electrical shock administered to psychiatric patients.

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Procedures

There were 17 subjects in this series, 6 men and 11 women. The mean age was 52 years, with a range of 21 to 77 years. Nine suffered from endogenous depression, three from schizophrenia, four from psychoneurosis, and one from a paranoid state probably resulting from an early arteriosclerotic dementia.

On the morning of treatment the overnight urine was discarded and two glasses of water were given. From then on all urine was saved until ECT, just before which the bladder was again emptied. This pre-ECT period was about two hours. After ECT the urine was again saved for four hours, the patient being asked to void at the end of this time to complete the post-ECT collection. During the latter period food and fluid were allowed, with the exception of coffee and tea. This procedure was performed once with eight patients, twice with six, and on 5, 6, and 13 occasions with each of the remaining three subjects, respectively, yielding a total of 44 administrations of ECT.

Clinical Outcome.—The attending and resident psychiatrists in charge of the clinical treatment were asked to assess in the following way the outcome of therapy one month after the patient's discharge from hospital:

1. Complete recovery (no symptoms, return to work and premorbid activity)
2. Much improved (free from symptoms)
3. Improved (symptoms less marked)
4. Unchanged
5. Worse

A similar assessment from the case record was made independently by one of us. Categories 1, 2, and 3 were classed together as "improvement" and Categories 4 and 5 as "no improvement"; concordance of the three estimates was required. If

readmission was required during this time, the patient was automatically classified as unimproved.

Pyrocatechol Amine Determination.—Pyrocatechol amines were estimated chemically by a procedure[8a] utilizing modifications of the extraction method of Euler and Orwen[9] and the fluorimetric method of Lund.[10] Rates of excretion are given as millimicrograms (mγ) of pyrocatechol amines (estimated as arterenol) per minute.

Statistical Methods.—Standard methods of statistical analysis were employed.[11]

Results

The rates of excretion of pyrocatechol amines were subjected to an analysis of variance, as shown in the accompanying Table. It may be seen that the differences in rate among patients were highly significant statistically, and also that ECT apparently brought about a lowering of the rate. This latter finding, though formally established, is probably of limited physiological significance, because the average rate was actually lowered in only nine patients after ECT, or on only 23 out of the 44 occasions that ECT was given. Moreover, the depression of the rate was not consistent for given patients tested on more than one day.

Two characteristics of the subjects were examined further: sex and outcome of treatment. The difference in rate of output of pyrocatechol amines between the sexes was not significant. However, it was found that patients who were adjudged to have improved according to the criteria employed in this study had exhibited an average rate of excretion of 40.2mγ/min., whereas those who did not improve excreted 63.4mγ/min., and the difference between these two rates was highly significant.

Analysis of Variance of Rate of Excretion of Pyrocatechol Amines in Urine of Seventeen Patients Treated by ECT

Sources of Variation	Degrees of Freedom	Mean Square	*F* Ratio	Significance (*P*)
All	87			
Subjects	16	2760	2.744	<1%
Sex	1	51	<1.0	>5%
Outcome	1	8304	8.256	<1%
Effect of ECT	1	6540	6.502	<5%
Remainder	70	1020	(1.000)	

Means:	Category	Rate, mγ/Min.
	Sex	
	Males	46.5
	Females	44.9
	Outcome	
	Improved	40.2
	Not improved	63.4
	ECT	
	Before	48.6
	After	42.4

Comment

Electroshock therapy did not alter the urinary excretion rate of pyrocatechol amines in either direction consistently, some patients showing an increased rate, and others a decreased one, after application of the current. Moreover, the direction of the change was not even consistent for patients tested on two or more occasions. Thus, the method employed here was unable to yield confirmation of sympathoadrenal stimulation initiated by ECT. It is important to note that the stimulation observed by Weil-Malherbe,[6] were it occurring under the present conditions of ECT, might not find its reflection in the urinary output of pyrocatechol amines. For example, increased circulating sympathetic amines might be withdrawn from the blood by tissues, so that the net effect on the urinary rate of excretion would be variable, depending upon specific conditions obtaining at the time of treatment or upon other factors which were not controllable. Actually, tissue absorption of pyrocatechol amines has been demonstrated with several organs, the diaphragm,[12] the heart and liver,[13] and the adrenal gland[14]; others may participate in this process. Alternatively, the released amines may be rapidly oxidized by amine oxidase or other enzymes to products not detectable by the chemical method used in this work.

The finding that those patients with a higher pyrocatechol amine excretion rate tended not to improve with ECT enabled us to predict retrospectively in a blind study the correct clinical outcome in 13 of the 17 patients. Although a higher pyrocatechol amine output may be indicative of manifest anxiety, clinical estimates were not fully in accord with such an explanation. Moreover, pyrocatechol amine output did not appear to be correlated with diagnosis. In view of

the empirically observed poor response to ECT of patients with predominating anxiety, this aspect remains to be further explored.

The results of this study indicate that the rate of excretion of pyrocatechol amines in the urine may provide a valuable prognostic tool. However, it is considered that the true importance of such a technique probably lies in the increase in our understanding of the basic physiological processes involved in the therapeutic change with ECT.

Dr. R. A. Cleghorn gave his encouragement in this work.

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Significance of Preexperimental Studies in the Psychosomatic Laboratory

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Introduction

It is traditional in medical research to utilize measurements of "basal states" as part of experimental procedures. The subject is first observed in a period of assumed stability and then again after the introduction of an agent that presumably alters the particular system under investigation. Comparison of responses under these two conditions may reveal the effect of the experimental agent. Psychosomatic research has also used this method, particularly in the so-called stress experiments. However, difficulties arise when the assumption is made that the "basal state" literally signifies that the subject is physiologically and psychologically at rest.

As Kaplan [1] has recently shown, "ordinary" medical laboratory procedures may constitute an emotional stress for uninformed subjects. The experimental setting is more threatening to the subject who has only a vague conception of the procedure. Often he meets new personnel, enters a strange room, and is exposed to complex apparatus. When a psychiatric inpatient serves as the subject for study, additional problems complicate responses to the experimental setting. The results of the total experiment cannot be understood without taking the personalized initial responses to strange people and procedures into account.

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From the Institute for Psychosomatic and Psychiatric Research and Training of the Michael Reese Hospital.

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In this paper we shall draw upon data from a multidisciplinary study of psychiatric patients in which the experimental design included techniques to assess the initial psychological and physiological responses during a preexperimental day* in the laboratory for a period of acclimatization to the procedure. Although it was anticipated that this would not be a "basal" day, several aspects of the quality and quantity of the responses were unexpected and appear to be relevant to the problem of obtaining adequate controls in psychosomatic studies. The focus of this report will be on the psychological and endocrinological findings during the preexperimental observation.

Subjects

The present report† deals with 22 experimental subjects, of whom 21 were hospitalized patients at the Institute for Psychosomatic and Psychiatric Research and Training of Michael Reese Hospital. The remaining subject was a university student who had been previously studied at the Institute. The average age of the patients was 38 years, with a range from 20 to 58. There were 13 men

* Throughout this paper the initial day in the laboratory will be referred to as the "preexperimental day." This is to be differentiated from the following three days in the laboratory, each of which involved the utilization of an experimental stress. These latter three days will be called either "experimental days" or "stress days."

† This paper is one of a series of publications which deal with an experimental approach to the problems of anxiety. The first publication [2] discussed the theoretical basis for such an approach and gave the background for the specific methods applied by the various specialties within the multidisciplinary group. Other papers will amplify certain details that have been presented in summary form in this paper, as well as other aspects of the project.

and 9 women in the group. They stemmed predominantly from middle-class families, and the majority paid for their private psychiatric care. Patients were selected for this study who either were prone to develop anxiety or had a significant degree of free anxiety as a major component of their symptom pattern. They constituted a group of diverse clinical entities, although "anxiety state," "agitated depression," and "borderline character disorder" were the most frequent admission diagnoses. A subject was chosen weekly from the available inpatient population and tested for four days. The experimental design limited the range of the patient sample because the subjects were required to remain seated in a chair for several hours consecutively and, at times, they were left unattended in the experimental room. Thus, grossly psychotic patients and subjects whose anxiety impelled them to move about could not tolerate such conditions.

Of the 22 subjects, 19 completed the entire week of testing. Three subjects who either were already too disturbed or were upset severely by the procedure were withdrawn from participation. This report will deal primarily with the 19 subjects who completed the experimental procedure.

Method

Consent of the subjects and their attending psychiatrists was obtained prior to testing, so that participation was voluntary. The patients were told that they would undergo tests which involved measurements of psychological and physiological responses and that they would be asked questions about their feelings in order to help us understand how their bodily functions responded to different emotional conditions. They were assured that all the resulting information would be made available to their doctors and might be helpful in their therapy. Each patient was informed that, although the procedure constituted research, he might obtain direct benefit from it, as well as some altruistic satisfaction.

On the preexperimental day an early-morning blood sample was drawn on the nursing unit for the purpose of measuring the plasma level of hydrocortisone. In addition, a 24-hour urine collection was started for measurement of urinary hydroxycorticoids.[3] Following these procedures the subject was brought into the testing room, electrodes were attached to his legs and wrist, and a respiratory band was placed around his chest.

After a short period, during which the subject sat alone in the experimental chair, two investigators entered the room and administered a test of perceptual discrimination, our so-called Area Judgment Test, for which the subject was required to decide which of two paired squares was the larger.[4] Following this another blood sample was drawn. Next in sequence was a psychiatric interview, in which an attempt was made to assess the patient's current reactions to the procedure, apparatus, and personnel. The interviewer was one of two psychiatrists who watched the entire procedure through a one-way vision screen.

Fig. 1.—The subject is seated alone in the experimental room while continuous physiological and observational records are being made.

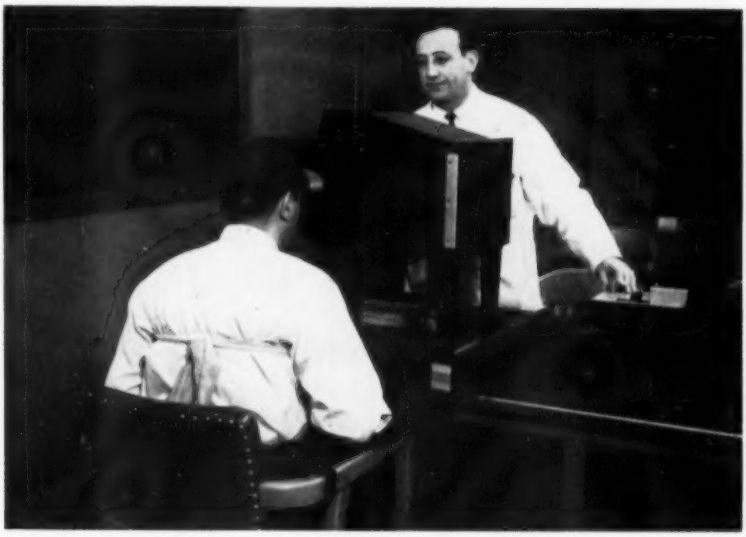
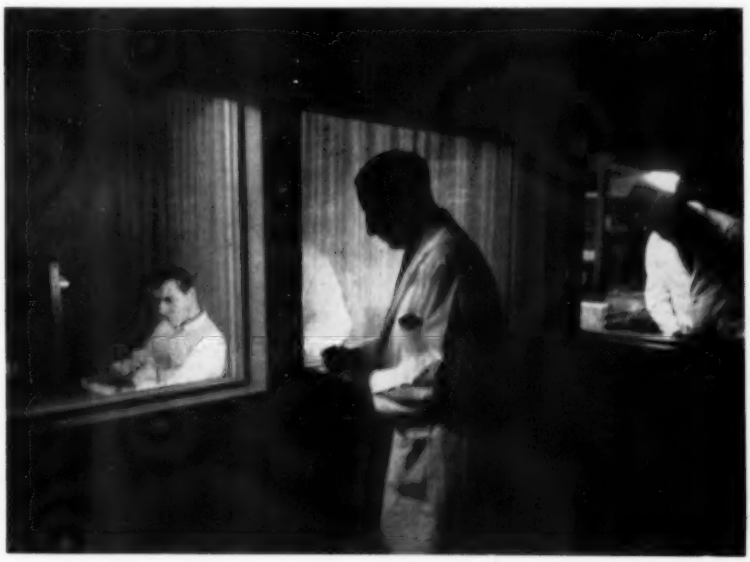


Fig. 2.—The Area Judgment Test is administered.

Figures 1, 2, and 3 are photographs of the laboratory. In Figure 1 the subject is seen seated in the experimental room. A respiratory band is shown around his chest, and an electrode strap is visible over his left wrist. In Figure 2 the subject is looking into the viewing box (tachistoscope), while taking the Area Judgment Test. To his left there is part of the one-way screen, which to the subject appears as a long rectangular mirror. Figure 3 shows one of the observers viewing the procedure through the one-way screen and making notations about the patient's behavior. The technician is visible in the background watching the physiological recordings on the oscillograph.

From their behavioral notes the two psychiatric observers make independent ratings of the patient's

Fig. 3.—The observer records behavorial notes while viewing the subject through a one-way screen.



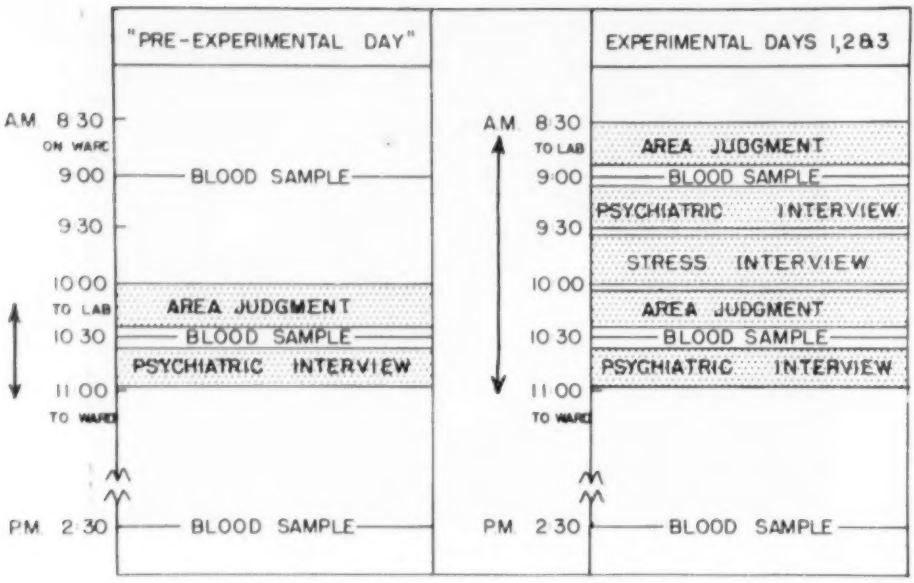


Fig. 4.—Experimental schedule for preexperimental and experimental days.

affective responses during the testing period. Each day at the conclusion of the experiment a consensus is determined from the individual ratings after a discussion in which each observer presents the basis for his ratings; either a compromise is reached, or one of the two ratings seems to be more accurate. Anxiety, anger, and depression were each rated on a 7-point scale, ranging from 0 to 6. A rating of 0 for anxiety means the absence of free anxiety, as, for example, in a healthy, well-integrated person not under stress. A level of 1 indicates distinct feelings of dread and apprehension which are well under control. A rating of 4 for anxiety usually impels the subject to motoric activity, such as pacing, which if sustained precludes the normal continuation of the experiment. Ratings for anger and depression are made on a similar 7-point scale. All ratings are based on (1) verbal communications to the interviewer regarding experienced affect and (2) nonverbal communication of emotional experience through signs, such as trembling, excessive sweating, changes in facial expression, and posture.

Following the preexperimental day the subject participates in three additional days of experimental testing. Figure 4 illustrates the design of these days as compared with the initial, or preexperimental day. Description and rationale for this experimental design has been presented elsewhere.[8]

Results

I. Psychiatric Observational Data

A. Affective Ratings.—The ratings of the level of anxiety for the preexperimental day and the three experimental days are shown in Figure 5. The mean anxiety for all occasions is slightly above the 1.0 level on the rating scale. On the preexperimental day the anxiety level is as high as any point reached on the subsequent experimental days.

The ratings for anger are very close to those for anxiety in the over-all mean, but the levels of anger on the preexperimental day are low (Fig. 6). Depression ratings are also relatively low on the preexperimental day as compared with the anxiety ratings (Fig. 7).

B. Varieties of Interpretation of the Laboratory Setting.—The affective ratings cannot do justice to the qualitative aspects of responses to the procedures. It became clear early in our research that any one of the component parts of the experimental

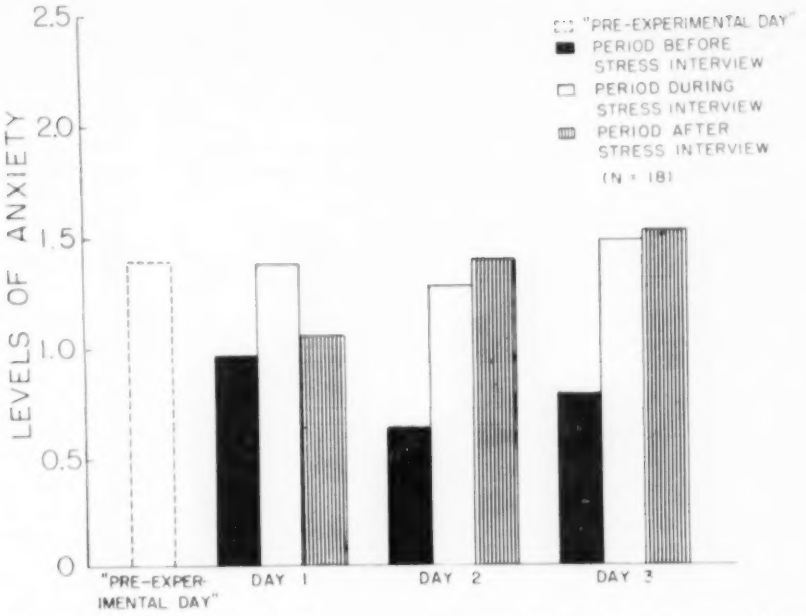


Fig. 5.—Group A: Levels of anxiety on preexperimental day and three experimental days.

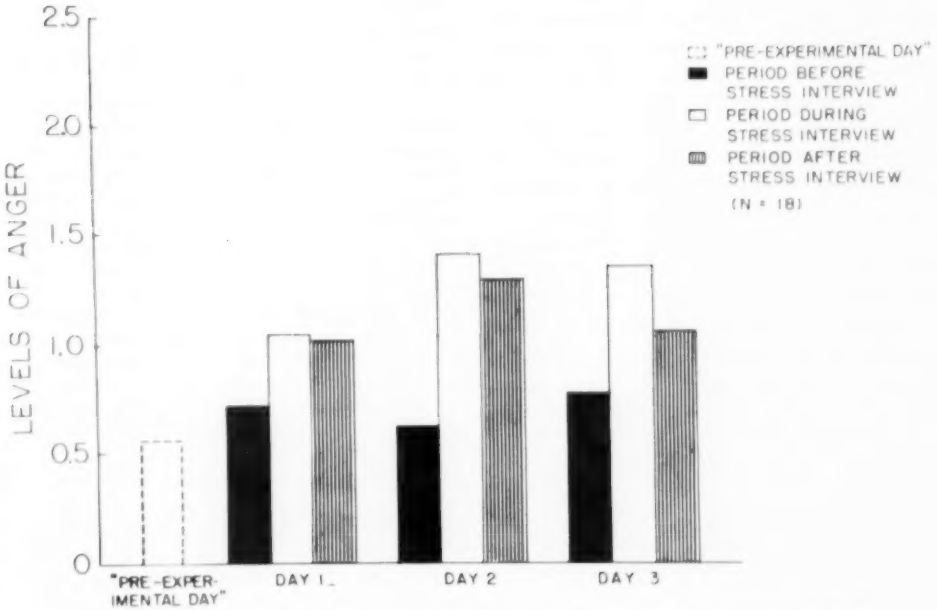


Fig. 6.—Group A: Levels of anger on preexperimental day and three experimental days.

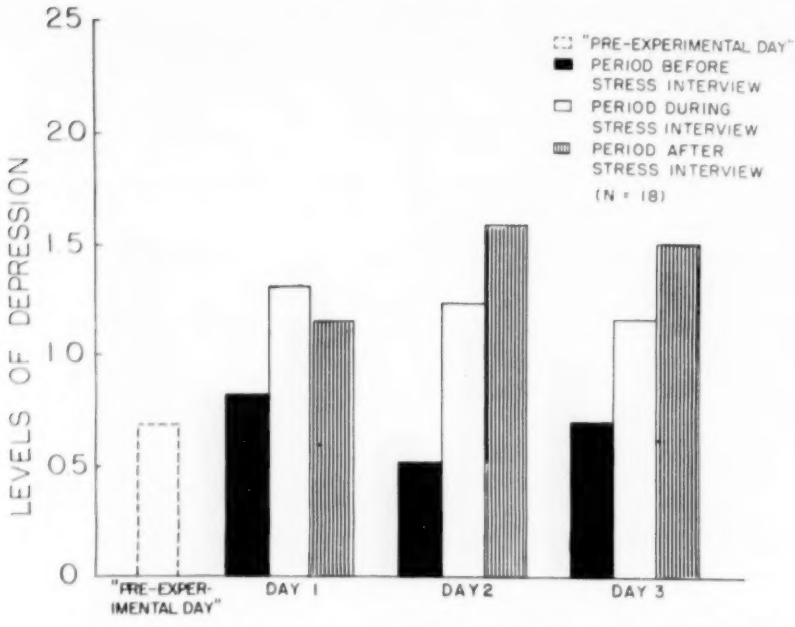


Fig. 7.—Group A: Levels of depression on preexperimental day and three experimental days.

setting could be described as stressful by the patients. At different times the viewing apparatus, mirror, blood drawing, decision making, immobilization, or interaction with the investigators served to evoke anxiety, depending on the significance of these cues for the unique conflict areas of the individual subject. On the other hand, several patients responded to the procedure with hopefulness or pleasurable affect. Following are a few vignettes of patient responses on the preexperimental day of testing which illustrate the variety of interpretations of the experimental situation.

Group I: Patients Who Responded with Emotional Distress or Unpleasant Affect

Case 1.—*Anxiety response to decision making and phobic reaction to the laboratory equipment*

A 49-year-old man was hospitalized for severe obsessive-compulsive symptoms and phobias for rabies and tetanus. During the Area Judgment Test on the preexperimental day he became concerned about the testing apparatus, felt that it was a carrier of tetanus and possibly might also produce rabies. He would not follow instructions for the Area Judgment Test by responding with one word, as it was very difficult for him to "commit" himself by making a decision. The free anxiety, however, was judged to be relatively low, probably because the patient utilized his familiar phobia as a defense against whatever anxiety the preexperimental day evoked.

Case 2.—*High anxiety response to being alone in the experimental room*

This 41-year-old woman, who entered the hospital because of agitated depression and conversion symptoms, illustrates an intense response to the parts of the procedure in which she was alone in the experimental room. When she began to fantasy abandonment, she felt immobilized by the respiratory band, which in fact was nonconstricting. She showed increasing signs of concern over the apparatus, felt smothered, and was increasingly anxious. At the peak point of anxiety she began to hallucinate. She indicated intense dread of the procedure, including both the personnel and the apparatus. This patient was rated as very high in anxiety, and because the study was too traumatic her participation in the experiment was discontinued after the preexperimental day.

Case 3.—*Apprehensive response to test objects*

This patient entered the hospital because of recurrent agitated depression and attacks of panic. Obsessive-compulsive defenses and hyperactivity relieved his periodic distress. This patient responded to the Area Judgment Test with anxiety, stating that he was quite apprehensive at first be-

cause he expected to be shown nude women on the test screen. He was anxious lest this happen but also disappointed when he saw the rather prosaic squares. He also became anxious when left alone in the room, expecting that he might be attacked in some unknown manner. A towel used during the drawing of blood stimulated his obsessive doubts, and he repeatedly asked if it had been sterilized.

CASE 4.—*Anxiety over electrocution in the experimental chair*

This patient showed a response common to most subjects. He became concerned about the electrical apparatus and wondered if he had been placed in an electric chair. He anticipated being shot and was constantly on the alert for this possibility. He was also disturbed by the rather impersonal roles assumed by the testers.

Group II: Patients Who Responded Predominantly with Hopeful or Pleasurable Responses

CASE 1.—*The procedure viewed as relief from boredom*

A 47-year-old woman had entered the hospital with a diagnosis of hysteria. In contrast to many of the patients, she enjoyed the preexperimental day. She especially liked the contact with a large number of new people and viewed the procedure in the context of providing relief from boredom. Thus, she stated that the novelty of the testing was somewhat pleasurable, even though she had some mild anxiety about the apparatus. In contradistinction to most of the subjects, she became disturbed as she "adapted" to the test setting, because then she became bored.

CASE 2.—*The procedure viewed in a therapeutic context*

A 34-year-old woman entered the hospital because of a severe obsession that she might harm her 7-year-old daughter. Although she was slightly tremulous and fearful that the apparatus might be used as a lie detector, she saw the procedure in a very hopeful context. She had had little contact with her psychiatric therapist, and she was very eager, almost desperate, for help. She viewed the study as an opportunity to reach out and contact people. On the preexperimental day she showed maximal expectations of benefit from the procedure.

II. Biochemical Observational Data

Plasma hydrocortisone levels in a normal control group are compared with the findings of the patient group on the preexperimental day (Fig. 8). The normal group,

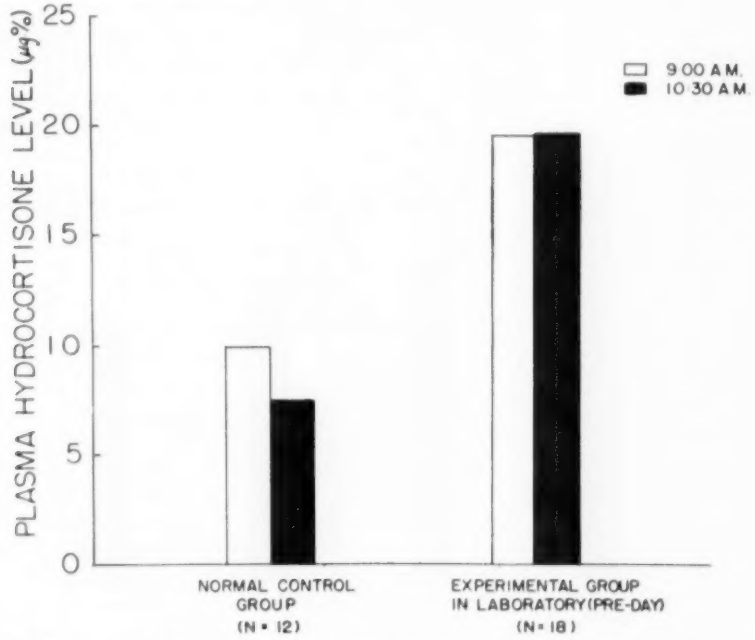


Fig. 8.—Plasma hydrocortisone levels: Anxious subjects (Group A) on preexperimental day compared with normal group.

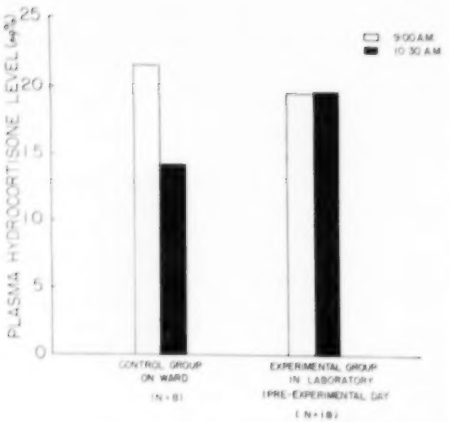


Fig. 9.—Plasma hydrocortisone levels in anxious subjects (Group A): Ward control group versus experimental group on preexperimental day.

consisting of hospital personnel, shows the usual hydrocortisone level, and its diurnal pattern was reported in several laboratories in addition to our own.[3,5,6] Plasma hydrocortisone tends to decline during the day from an early-morning "high." However, patients on the preexperimental day start at a significantly higher level of plasma hydrocortisone than normals. Furthermore, they fail to show the expected fall in level by 10:30 a. m.

The experimental group on the preexperimental day are compared with a control group of anxious subjects studied on the hospital units (Fig. 9). The control patients were chosen to be as near like the experimental group as possible. The 9:00 a. m. blood specimen in both groups were drawn on the units, but the later sample was taken from the experimental group in the laboratory. The initial levels do not differ significantly, but the anxious control group not exposed to the experimental setting shows the expected diurnal fall, while the hydrocortisone level of the experimental group fails to show this decline.

Figure 10 compares the plasma hydrocortisone levels on the preexperimental day with those found on the "stress days." The findings on the preexperimental day differed in that the expected diurnal variation does not occur.

The 24-hour urinary hydroxycorticoids were significantly higher than a normal con-

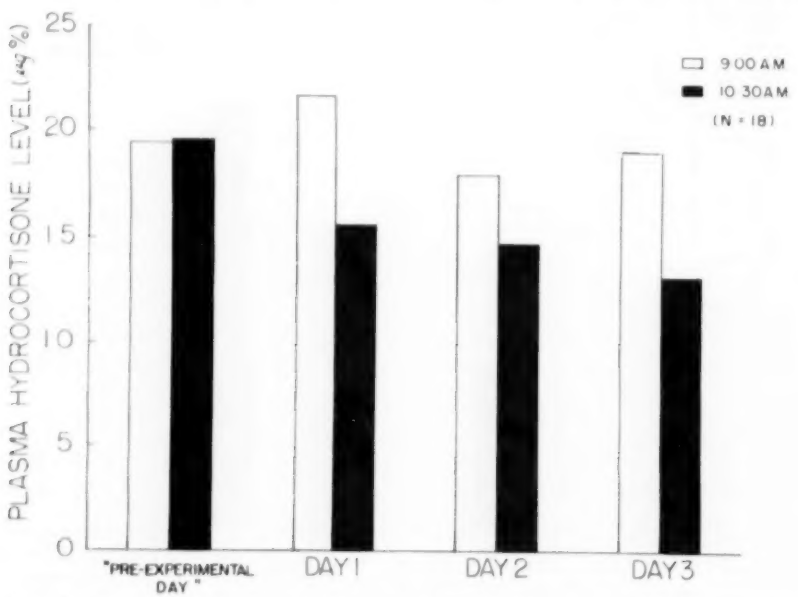


Fig. 10.—Plasma hydrocortisone levels in anxious subjects (Group A): Preexperimental-day levels compared with experimental-day levels.

trol group on each of the four days of testing. The levels of the patient group approximate the levels found by Hill et al.[7] in their study of Harvard crewmen on the day of "the big race." The urinary hydroxycorticoids on the preexperimental day were higher than the levels found on the experimental days, but the difference did not achieve statistical significance.

In summary, the biochemical data yielded the following three types of results:

1. Values in which there is significant difference between the preexperimental day and the three experimental days. This is seen in the reversal of the usual diurnal plasma hydrocortisone fall on the preexperimental day.

2. Values which were abnormal on the preexperimental day and also on the three experimental days without significant difference. This held for the 24-hour urinary hydroxycorticoids, which were abnormally high each day as compared with values for a normal group. It is also true of the plasma hydrocortisone levels, which were significantly higher than those of a normal control group on all occasions.

3. Other values[3] which were normal on the preexperimental day and also on the three experimental days.

Comment

I. Why Is the Initial Day So Stressful?

A. Specific Threatening Implications.—The patient has some information pertinent to the laboratory study he is about to undergo, and much of this information has threatening implications. In the first place, he knows he is a patient in a mental hospital. In the second place, he knows that something is going to be found out about him, since these tests are presented as thoroughgoing explorations of mental and bodily functions. Taking these two bits of information together, the patient is very likely to be concerned with the possibility of discovering that his condition is more serious than he had previously been told. The stage is set for him to discover in the tests almost anything that he might imagine about himself. While his wishes for encouraging news may be stimulated, his worst inner fears may be confirmed as well. Since only a minority of the patients in the hospital underwent these testing procedures, the patient might well raise the question why he was being selected for this study. It seems only a short step from this question to the concern that the reason for selection might be a suspicion on the part of the medical staff that his condition is particularly severe or potentially dangerous.

Once in the laboratory, the patient experienced a significant change from the accustomed routine of the hospital. In the first place, he had become accustomed to friendly, communicative, helpful behavior on the part of staff members. In the laboratory, however, because of the plan of the experiment, everyone with whom the patient came in contact was (deliberately) impersonal, unresponsive emotionally, and minimally communicative. In addition, the laboratory was rather formidable physically, with its complicated equipment, wires, and odd chair. For many patients, the equipment had some implication of physical danger, though the intensity of such concerns varied greatly.

Parenthetically, it is informative to consider the traditional distinction between fear and anxiety in light of the patients' emotional reactions to the laboratory equipment. Ordinarily, this distinction is based primarily on the source of the emotional experience. When there is a clear and present danger in the current environment, the emotion is called fear; when the same feeling state occurs without a discernible danger in the external environment, we say the person is experiencing anxiety and the source of the danger is within himself. At these extremes, the distinction seems useful. It appears, however, that there is a continuum from fear to anxiety, and that most of the significant experiences of ordinary life and of clinical practice fall within the middle range, where the tradi-

tional distinction between fear and anxiety is not so easy to make. In these instances, the terms fear and anxiety tend to be used interchangeably. This may be illustrated in the present study by the patient's frequent response to the chair and wires with some feelings of apprehension, foreboding, or dread. At first glance it may appear that this is a simple case of fear in the traditional sense. After all, many persons in our culture learn to associate a wired chair with an electric chair and hence with danger. Thus, the patients are responding realistically to a culturally defined dangerous stimulus in the current environment. There is some truth to this; yet the case is not so simple. For one thing, a plain wooden chair in a hospital laboratory and a set of wires do not make a prison-style electric chair. Furthermore, the reactions of different subjects to this chair differ greatly, even though many see some sort of potential danger in it. The nature and extent of the danger is viewed quite differently by different patients. They, in fact, interpret this chair in light of past experiences and personal meanings, including unconscious ones. Thus, there is a nucleus of real environmental danger and an elaboration of this danger in terms of the subjects' past experience and inner tendencies. In terms of the traditional distinction, then, there are both fear and anxiety fused in the patient's response.

B. Novelty, Ambiguity, and Preparation

The finding of relatively high anxiety and steroid levels on the initial day in the laboratory also touches on the more general question of the threat inherent in novelty itself. Since they had never been in this laboratory and had never undergone these procedures before, they were in a sense unprepared. It might well be that new experiences are intrinsically stressful, because the subject is fundamentally unprepared for the events he is about to experience. Certainly, there is evidence from recent studies which is quite consistent with our data and suggests the stressful nature of first experiences. A previous study from this Institute presented evidence indicating impairment of perceptual discrimination in older subjects under the impact of a novel, ambiguous laboratory situation.[8] Mason and co-workers[9,10] have shown that plasma hydrocortisone elevations are associated with the first handling and venipuncture of a new monkey and the first transfer of a monkey from his home cage to an experimental cage. Reiser and associates[11] found significant abnormality in cardiovascular function in a group of soldiers on their first experience in a laboratory similar to our own. Indeed, Reiser's data suggest that a verbal preparation at the outset of the procedure has surprisingly little effect in terms of mitigating the stress-type cardiovascular and emotional responses. This raises the question whether the novelty in itself is sufficiently threatening that words alone do not suffice to give the subject full security from a psychosomatic viewpoint.

These findings are reminiscent of Hebb's study,[12] in which he showed the existence of spontaneous fear of strangers in infant chimpanzees. He says:

> The growing chimpanzee is persistently afraid of strange persons, objects and places, although the response is not always predictable in the individual case. . . . The fear of strangers by chimpanzee infants is spontaneous and cannot be accounted for as a conditioned response. Also a slight change of clothing may produce fear of a familiar attendant who was not feared before. . . . Strange chimpanzees are feared as much as strang men. . . . Fear of strange persons is not determined by a particular property of sensory excitation but by some discrepancy of pattern from those which have been frequently experienced by the subject. . . . Unexpectedness is an essential feature of a number of fear provoking situations.

Several workers have presented interesting observations on fear of strangers in human infants.[13] Here, again, there seems to be an early appearance of behavior indicating that the new and strange evokes at least responses of alertness and caution and sometimes considerable emotional disturbance. Thus, it seems that there may well be a long-standing and deep-going orienta-

tion in man to regard the new and strange as potentially dangerous.

Yet, at the same time, we should not overlook some of the gratifying and often constructive aspects of novelty in human experience. There is an adage to the effect that "novelty is the spice of life," and it does not take much observation of American life to conclude that the quest for novelty is indeed an important part of the picture. For many people new experiences are stimulating, gratifying, and even an essential part of living. Thomas,[14] a good many years ago, described the wish for a new experience as one of the basic tendencies in human behavior. Children, during the early years of life, spend an enormous amount of energy in exploring and manipulating new objects,[15,16] and much of this appears to be satisfying to them. Harlow[17] and associates have shown dramatically the importance of curiosity, exploration, and manipulation in behavior of monkeys. The motivation of monkeys for experiences of this kind appears to be very great.

Thus, there is a positive side to new experiences, as well as a negative one. They are often stressful; and yet they may well be highly gratifying. In any comprehensive account of the psychosomatic significance of new experience, both aspects must be taken into consideration. It seems that human beings want new experiences and yet fear them. It seems possible to resolve this apparent paradox by stating that we seek novelty within a basic framework of familiarity and stability. Novelty may well be gratifying when bodily integrity and essential values are not in jeopardy. When a person feels quite confident that the basic features of his life are secure and continuous, he may well find stimulation, excitement, pleasure, and achievement in experimenting with new persons, new places, new activities, and new objects. It is usually necessary for the individual to maintain the stable framework of his life, even if this requires some self-deception. For many of the patients in this experiment, the framework itself was not secure, since the setting and structure of the experiment implied a challenge to his basic values—for example, his mental and physical health and his relations with other human beings.

II. The "Basal State" in Psychosomatic Research

There are a great many studies in the psychosomatic literature which rely upon a comparison of two measures made under contrasting conditions: a basal, or resting, measurement *vs.* a measurement following a specific experimental intervention. Frequently the basal measurement is obtained on the first contact with the patient and the experimental measure on the second contact. In the basal measurement, the patient is nearly always at rest physically, but frequently little is said about his emotional state. This procedure appears to be a carry-over from other fields of medical research, where it has become a customary practice in clinical experimentation. The data of this study point to a serious limitation in this type of procedure. The initial day of testing (preexperimental day) is not always "basal"; on the contrary, it may be quite stressful, as we see in this study. Indeed, the results of the present study, as well as the recent work of Reiser and of Mason, point up the need for systematic research on the psychophysiology of novelty and ambiguity.

When investigators study a physiological or psychological process which is likely to be influenced by anxiety, it is desirable to compare a "basal" (anxiety-free) measurement with a measurement following experimental intervention. For such purposes, it is probably necessary to observe the subjects on two or three occasions of measurement until they are thoroughly acclimated to the laboratory situation. An alternative procedure would be to put the "basal," or "resting," study at the end of the experiment, when the whole procedure has become thoroughly familiar to the patient. Either of these plans prolongs the experiment and

may lead to other emotional complications—for example, resentment, boredom, or discouragement in the patient, each of which may have physiological ramifications.

It does seem possible to adjust to the laboratory setting even in one day, at least as far as the disappearance of emotional distress is concerned. In our patient group there was a sharp drop in anxiety from the initial preexperimental day to the start of the next day, i. e., the first stress interview day. The advantage of allowing this time for adaptation to the laboratory is that it tends to separate stress effects of the laboratory situation from experimentally induced and intended stress. If, for example, a rise in anxiety or hydrocortisone occurs on the second or third experimental day, this can more likely be attributed to the intended stress than to the laboratory itself.

It should be noted, however, that not all studies require basal measurements. The purpose of control conditions is not necessarily to have measures representing utter quiescence. For many purposes it is quite sufficient to have a measure in which all "natural" variability occurs, that is, the variability of a given system if it is under the usual conditions of its functioning. This can then be contrasted with an especially designed condition in which an intentional effect is produced. If there is considerable variability in the system under study and/or relatively small effect from the experimental intervention, longer and more exacting control measures must be taken, approximating basal conditions. If, on the other hand, the system is ordinarily a very stable one and the experimental condition produces a relatively large change in it, then less stringent controls are adequate. There have been many papers in the psychosomatic literature in which an emotional crisis is shown to be associated with such a major change in the functioning of a physiological system that it makes little difference how near to quiescence this system was previously. The difficulty lies, however, in the fact that many psychosomatic processes involve small changes, though perhaps prolonged or frequently repeated ones. If these small changes occurring under the impact of day-to-day emotional experiences are to be detected reliably, it is very helpful to have a contrasting condition which very nearly approaches emotional quiescence, as well as physical rest. It is in this type of problem that investigators must use great caution in assuming that the initial contact with the patient is a basal one.

Summary

This report describes a multidisciplinary experimental study of anxiety and focuses on an initial, or preexperimental day in the laboratory in which psychological and physiological observations were made. We have shown that the process of acclimatization to the laboratory setting may constitute a special stress for the experimental subject. Anxiety was relatively high on the preexperimental day in the laboratory as compared with the subsequent three experimental days. In addition, plasma hydrocortisone showed a striking reversal of diurnal pattern on the first day in the laboratory. Urinary hydroxycorticoids were elevated above normal values on the preexperimental day but were not significantly higher than experimental-day values.

These results support the conclusion that a preexperimental day cannot be considered as a psychologically neutral condition for the assessment of a "basal" or "resting state," at least in the type of experimental population employed in this study. The importance of this view for psychosomatic and medical research methodology is discussed. Of equal importance, however, are the implications of these findings for the understanding of anxiety. Both the inherent novelty and ambiguity of the experiment and the laboratory situation, and the idiosyncratic meanings given it by the subject can constitute a psychological stress.

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Books

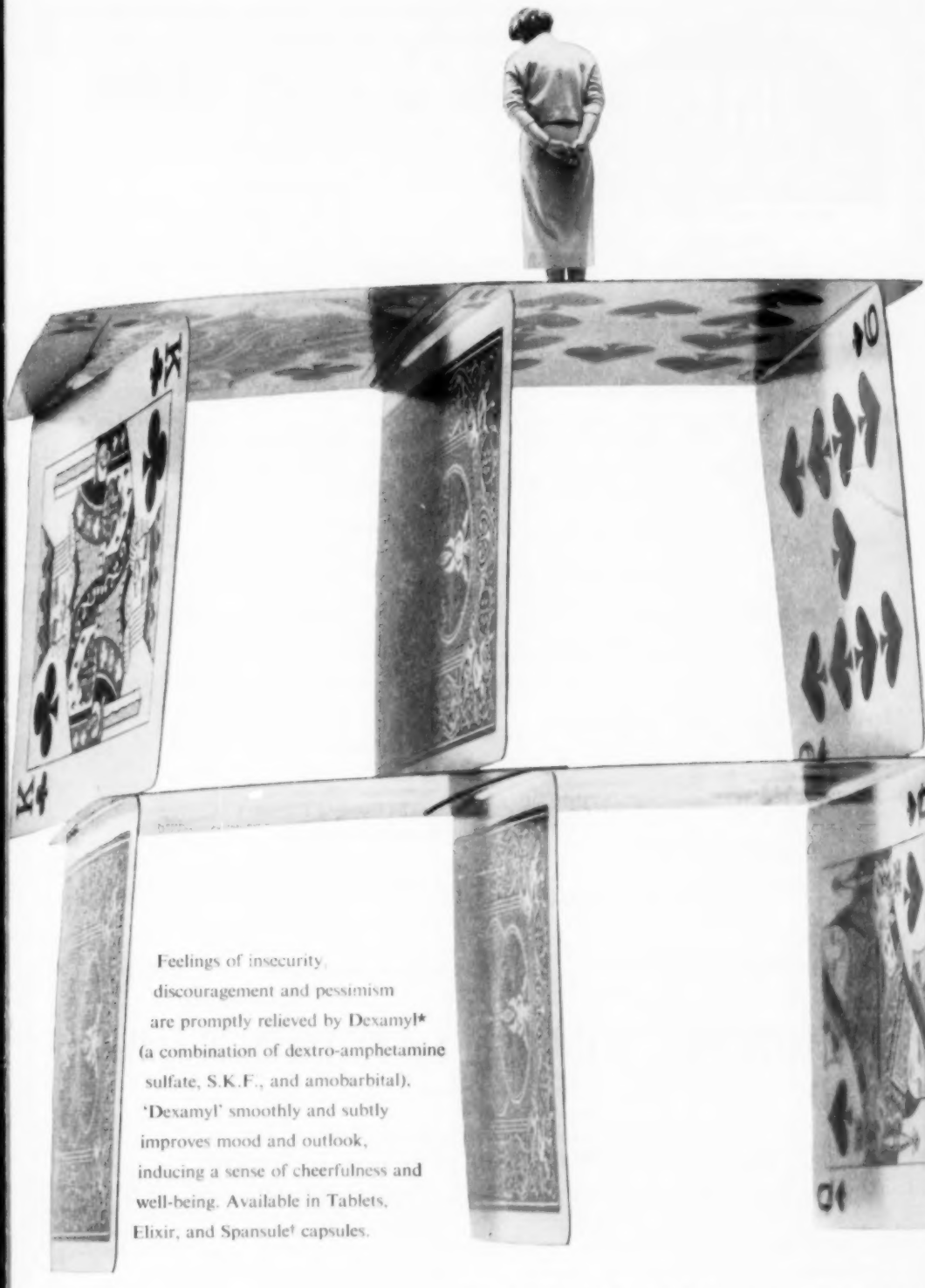
BOOK REVIEWS

Comparative Psychology of Mental Development. By Heinz Werner. Revised edition, second printing. Price, $6.00. Pp. 564. International Universities Press, Inc., 227 W. 13th St., New York, 1957.

A new printing of Werner's classic study again makes available a basic reference for all students of primitive thought processes. Although the work was published in English in the mid 1940s, the original research from the Hamburg Psychological Laboratories and the earlier German editions appeared during the preceding two decades. A pioneer work of admirable scholarship, the book continues to be a major contribution. The growth during these years of interest within dynamic psychiatry in problems of ego psychology and the thought processes should, if anything, enhance its present value.

The developmental psychology proposed by Werner attempts to integrate within one conceptual framework the behavior of the child, the primitive, and the psychotic. Drawing from a vast fund of information in the areas of child and animal psychology, studies of psychopathology, and cultural anthropology, the author demonstrates the essential continuity among these diverse groups in mental organization. In all, perception and conception, thought and action, are immediate, concrete, and utilitarian, marked by syncretism, animism, and magic. Inner needs and feelings are egocentrically fused with the perception of reality, and the concepts of time, space, and causalty are tied to the immediate world of action. With increased differentiation and organization, and the sharpening distinction of self and object, primitive thought evolves toward the abstract and scientific thought of civilized man. Though discrete modes, the prelogical and the logical are continuous, and transitions between them are small.

Even aside from the fertility of Werner's developmental theory, the vast amount of material presented, much of it drawn from European sources unknown to most American psychiatrists, makes this work invaluable, not only for those concerned with the systematic understanding of ego functioning and development but for all clinicians who daily see and seek to understand the residuals of earlier developmental levels in the mental functioning of their patients.



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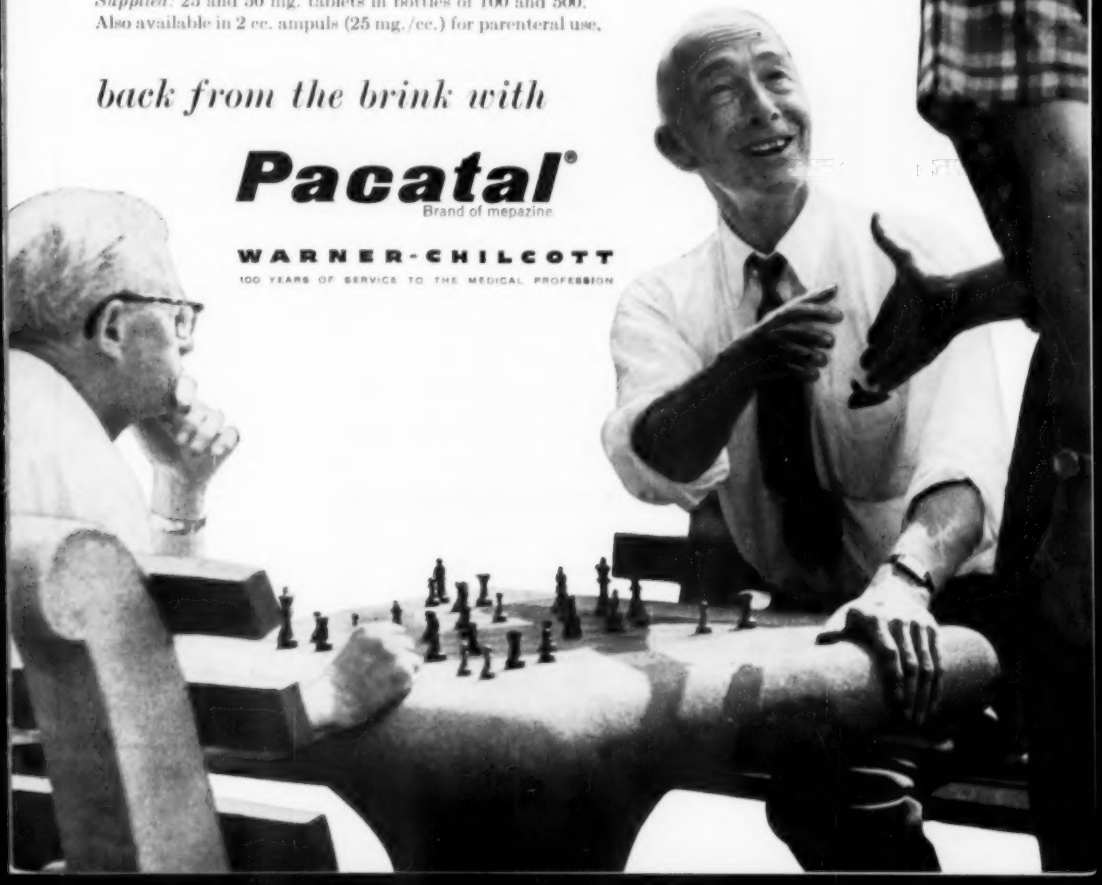

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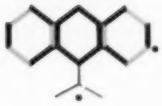

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